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Supramolecular Organometallics: Carbene Chemistry beyond the Molecule

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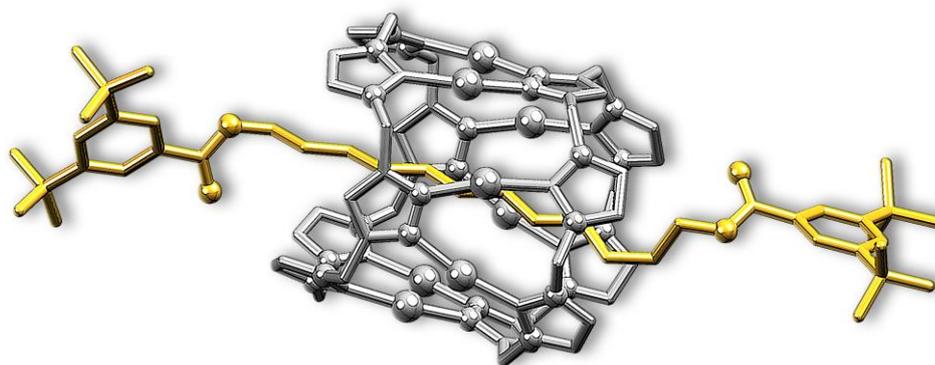
I feel a little bit like the Wright Brothers,
who were flying 100 years ago for the first time and then people were saying:
'Why do we need a flying machine?'
And now we have a Boeing 747 and an Airbus.
So that is a bit how I feel.

Bernard L. Feringa

Das Genie ist ein Blitz,
dessen Donner Jahrhunderte währt.

Knut Hamsun (1859-1952)

Für meine Familie & Carolin

Danksagung

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Deutsche Zusammenfassung

Vor dem Hintergrund natürlicher Prozesse, welche häufig auf komplexen nicht-kovalenten Wechselwirkungen beruhen, strebt die Disziplin der supramolekularen Chemie danach, diese faszinierenden intermolekularen Mechanismen nachzuahmen. Die Integration von metallhaltigen Komponenten bietet dabei eine Fülle an potentiellen Vorteilen. Eine für diesen Zweck geeignete Klasse organometallischer Systeme sind *N*-heterozyklische Carbene, da sie im Allgemeinen sehr stabile Komplexe mit vielen Metallionen bilden. Deshalb ist die Hauptmotivation dieser Arbeit die Verknüpfung der Konzepte von supramolekularer und organometallischer Chemie.

Dafür ist zunächst ein Ligandsystem erforderlich, das die einfache Synthese von Metallkomplexen mit derartigen Eigenschaften ermöglicht. Der erste Teil dieser Arbeit beschreibt die Synthese eines hybriden Imidazol/Pyrazol-Cyclophans als neuartiges Ligandmotiv, welches in der Lage ist, stabile, dimetallische Komplexe mit Nickel(II)ionen zu bilden. Anschließend werden Ligandmodifizierungen mit dem Ziel untersucht, die Form der Kavität für die Anionenerkennung in Lösung zu optimieren. Bereits kleine Veränderungen in der Peripherie des Liganden haben entscheidende Auswirkungen auf die Affinität der NHC-Komplexe für Halogenide. Eine perfekte Halbschalen-Struktur, in der zusätzliche Wasserstoffsubstituenten in den Hohlraum gerichtet sind, führt zur Bildung eines 2:1-Wirt-Gast-Komplexes mit Chlorid- oder Bromidanionen. Die Entstehung dieser „Capsoplexe" ist nicht koordinationsgetrieben und das Anion spielt eine aktive Rolle bei seiner Entstehung. Weitere Forschung in diese Richtung wurde mit dem Fokus auf der Isolierung von Intermediaten betrieben, die sich während der Synthese dieser Komplexe bilden, was für ein tieferes Verständnis der auftretenden Elementarschritte enorm aufschlussreich ist.

Der zweite große Fokus dieser Dissertation ist die Synthese der Münzmetallkomplexe (Ag, Au) mit dem hybriden, Imidazol/Pyrazol-basierten Liganden. Das starre M_8L_2-Gerüst mit seiner zylinderförmigen Kavität ist von perfekter Größe für die Aufnahme kleiner und unverzweigter Moleküle. Die Quantifizierung der Aufnahme linear Gast-Substrate durch die so genannten „Pillarplexe" zeigt, dass diese NHC-Komplexe nicht nur vergleichbare, sondern sogar höhere Assoziationskonstanten zeigen als etablierte organische, makrocyclische Wirtverbindungen. Die herausragende Affinität zu linearen Molekülen wird anschließend für die Synthese eines [2]Rotaxans ausgenutzt, das durch Reaktion eines inkludierten, langkettigen Diamins mit sterisch anspruchsvollen Stopper-Einheiten erhalten wird. Die mechanisch verzahnte Architektur wird in nahezu quantitativer Ausbeute erhalten und zeigt eine erhöhte Stabilität gegenüber saurer Zersetzung der organometallischen Wirtsverbindung verglichen mit normalen Pillarplexen. Diese Eigenschaft kann einem stabilisierenden „Rotaxand-Effekt" zugeschrieben werden, der die Zersetzung durch die Erhaltung der räumlichen Nähe zwischen den beiden Ligandmolekülen deutlich inhibiert. Zusätzlich kann das [2]Rotaxan mittels starker Säuren zu einem organischen [3]Rotaxan umgewandelt werden. Dieser Prozess ist durch Zugabe einer Base reversibel gestaltbar.

Diesen Ausführungen folgen zwei weitere Manuskripte, welche sich mit der Synthese, Charakterisierung und Reaktivität von verwandten Tetra(NHC)-Komplexen beschäftigt, sowie zwei Review-Artikel, welche im Zuge von Nebenprojekten während dieser Dissertation entstanden sind.

English Abstract

Against the background of nature relying on non-covalent interactions in an elaborated and highly complex way, the scientific discipline of supramolecular chemistry strives to mimic those fascinating intermolecular mechanisms. For this target, the incorporation of metal-containing components into such scaffolds offers a plethora of potential benefits. A promising class of organometallic systems for this purpose are *N*-heterocyclic carbenes, as they generally form exceptionally stable complexes with many metal ions. Consequently, the main motivation of this work is the marriage of these two concepts, namely supramolecular and organometallic chemistry.

Therefore, a ligand system is required that allows for the facile synthesis of the respective metal complexes with the desired supramolecular properties. Accordingly, the first part of the thesis describes the synthetic approach towards a hybrid imidazole/pyrazole cyclophane as a novel ligand motif capable of forming stable, dimetallic complexes with nickel(II) as central ions. Subsequently, ligand modifications are investigated in order to fine-tune the cavity's geometry for anion recognition applications. It is shown that minor changes in the periphery of the ligand have a decisive effect on the affinity of the NHC complexes for halides. A perfect half-bowl structure with additional hydrogen substituents pointing into the cavity leads to the formation of a 2:1 host-guest complex with chloride or bromide anions. The formation of these "capsoplexes" is not coordination driven and the guest plays an active role in the realization of the assembly. Further research in this direction is presented focusing on the isolation and characterization of intermediates that occur during the synthesis of these nickel complexes allowing for an in-depth understanding of the occurring elementary steps.

The second major focus of this dissertation is the synthesis of the coinage metal complexes (Ag, Au) featuring this hybrid imidazole/pyrazole-based scaffold. Their highly rigid M_8L_2-type framework with its central cylinder-shaped cavity is of perfect size for the uptake of small and unbranched molecules. Quantification of the association of the so-called "pillarplexes" with linear model guest-substrates suggests that these NHC complexes exhibit not only comparable, but even superior association constants in comparison to established organic, macrocyclic compounds employed for this purpose. The outstanding affinity to linear entities is exploited in the subsequent synthesis of a [2]rotaxane by reaction of a hosted long-chained diamine with sterically demanding stopper moieties. The mechanically interlocked architecture is feasible in nearly quantitative yield and exhibits an enhanced stability against acidic decomposition of the organometallic host compared to the normal pillarplexes. This feature can be attributed to a stabilizing "rotaxand-effect" that inhibits degradation by preventing a spatial separation of the involved ligands. Additionally, the [2]rotaxane can be switched to a purely organic [3]rotaxane by de-coordination of the metal centers and re-protonation of the ligand by strong acids. The process is reversible and upon addition of a suitable base the organometallic [2]rotaxane is recovered.

These descriptions are followed by two more manuscripts focused on the synthesis, characterization and reactivity of related macrocyclic and open-chain imidazole-based tetra(NHC) complexes, respectively, as well as two review articles that have been prepared within side projects carried out during the course of this dissertation.

List of Abbreviations

% V_{bur}	percent buried volume
Å	Ångström (10^{-10} m)
Ac	acetyl
Ad	adamantyl
ADP	adenosine diphosphate
ATP	adenosine triphosphate
BNAH	1-benzyl-1,4-dihydronicotinamide
Boc	tertiary butyloxycarbonyl
BTSA	bis(trimethylsilyl)amide
Bz	benzyl
CBPQT	cyclobis(paraquat-*para*-phenylen)
COD	1,5-cyclooctadiene
Cp	η^5-cyclopentadienyl
Cp*	η^5-pentamethylcyclopentadienyl
Cy	cyclohexyl
DCM	dichloromethane
DFT	density functional theory
DIPEA	diisopropylethylamine
Dipp	2,6-diisopropylphenyl
DMF	*N,N*-dimethylformamide
DMSO	dimethyl sulfoxide
DNA	deoxyribonucleic acid
DNP	dioxynaphthalene
DOSY	diffusion-ordered spectroscopy
E/D	epoxide to diol ratio
em	emission
EPR	electron paramagnetic resonance
equiv.	equivalent
Et	ethyl
ex	excitation
EXAFS	extended X-ray absorption fine structure
GSCC	ground state co-conformation
HOMO	highest occupied molecular orbital
Im	imidazole
^{i}Pr	isopropyl, propan-2-yl
IR	infrared
ITC	isothermal titration calometry
IUPAC	International Union of Pure and Applied Chemistry
K_d	dissociation constant
L	variable ligand
LDA	lithium diisopropylamide

LEP	Lever electronic parameter
LUMO	lowest unoccupied molecular orbital
M	variable metal
m	*meta*
m/z	mass-to-charge-ratio
*m*CPBA	*meta*-chloroperoxybenzoic acid
Me	methyl
Mes	mesityl, 2,4,6-trimethylphenyl
MIM	mechanically interlocked molecule
MOF	metal-organic framework
MS	mass spectrometry
MSCC	metastable co-conformation
MSTJ	molecular switch tunnel junction
μ^n	bridging (with n metals bound to the bridging ligand)
^{n}Bu	normal butyl, butyl
NHC	*N*-heterocyclic carbene
NHDC	*N*-heterocyclic di(carbene)
NMR	nuclear magnetic resonance
nwp	non-water-assisted pathway
o	*ortho*
OLED	organic light emitting diode
ORTEP	Oak Ridge Thermal Ellipsoid Plot
p	*para*
Ph	phenyl
ppm	parts per million
py	pyridyl
R	variable substituent
r.t.	room temperature
$T_{1/2}$	half-life
^{t}Bu	tertiary butyl
TEP	Tolman electronic parameter
Tf	triflyl
THF	tetrahydrofuran
thp	tetrahydropyran-2-yl
THT	tetrahydrothiophene
Tol	tolyl
TTF	tetrathiafulvalene
UV/Vis	ultraviolet visible
VT	variable temperature
wap	water-assisted pathway
X	variable leaving group or anion
XRD	X-ray diffraction
η^n	hapticity (over n continuous atoms)

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1 THE BROADER CONTEXT

The following chapter intents to outline the scientific playground which this work is situated in and highlights its scientific background, as well as selected current research directions and key developments.

1.1   Nanotechnology – Quo vadis?

"There's plenty of room at the bottom." This is the title of a famous lecture that physicist Richard Feynman gave in 1959 at the annual meeting of the American Physical Society at the California Institute of Technology.[1] With this lecture, he laid the conceptual cornerstone for the field now referred to as nanotechnology by imagining a future marked by miniaturization, its consequences and challenges. Exemplarily, he estimated that upon allowing $5 \cdot 5 \cdot 5 = 125$ atoms to contain one bit of information, all printed data accumulated over centuries since the Gutenberg Bible could be stored in a cube of material 0.1 mm wide, which is barely visible to the naked eye. The visionary scientist made numerous further suggestions, how technology might work on a microscopic level and years later, many of these concepts became the foundations of nanoscience. His thought experiments and ideas raised the central question how machine-like functionality can be translated from the macroscopic reign of gravity and inertia to microscopic dimensions where processes are governed mainly by Brownian motion and electrostatic interactions.

However, it took roughly 30 years until nanoscience really jumped off in the 1990s, driven by spectacular inventions, for example scanning tunneling microscopy, carbon nanotubes, or microchips shrinking in size, but growing in computing capacity at incredible rates. The areal density, in other words the number of bits per square centimeter, doubled approximately every 1.5 years during the last decades.[2] Accordingly, one bit of information occupies only several 100000 atoms on a modern terabyte harddisc. Given that this trend continues for another decade, Feynman's abovementioned thought experiment might eventually become reality. However, progressing into this nanoregime, where a few hundred atoms store and process information, grows ever more burdensome, such that harddiscs cannot be miniaturized infinitely. This is due to the fact that a single storage cell – an area of identical magnetization storing one bit of information – becomes increasingly instable upon size-reduction, caused by a thermally induced change of their magnetization and thus, loss of information. Additionally, addressing such small storage cells *via* magnetic fields is limited.[3] These challenges call for new approaches upon entering the nanoworld and chemistry as a scientific discipline operating on the molecular scale will certainly play a crucial role during this process. Designing discrete molecules that are able to store and retrieve information by external stimulation and implementing them into working circuits is only one of the ambitious ideas in a very interdisciplinary field of modern research.

A pioneering example that beautifully transcends the borders of research areas, was reported by Stoddart, Heath and co-workers in 2007.[4] They built a functional 160-kilobit molecular electronic memory patterned at 10^{11} bits per square centimeter by storing information on addressable molecules (Figure 1).[4] The core of the device consists of an assembly of Si bottom-nanowire electrodes crossed by Ti top-nanowires sandwiching a monolayer of bistable mechanically interlocked molecules **I-1** (MIMs, see chapter 1.2.2), which results in so-called

molecular switch tunnel junctions (MSTJs). Each bit corresponds to an individual MSTJ and contains approximately 200 of said molecules serving as the data storage elements. In the ground state the macrocyclic, cationic component of **I-1** (blue, Figure 1) encircles the tetrathiafulvalene (TTF; green, Figure 1) site cooresponding to the low-conductance '0' state. The electrochemical oxidation of TTF to its dication results in the translation of the macrocycle to the dioxynaphthalene (DNP; red, Figure 1) site due to Coulomb repulsion. The subsequent reduction of the TTF radical cation back to its neutral state leads to a metastable state where the ring component resides on the DNP unit despite having a higher affinity for the recovered, neutral TTF moiety which corresponds to the high conductance '1' state. The system subsequently relaxes back to the ground state by the return of the ring to the TTF station with a half-life of about an hour in the device environment.[4]
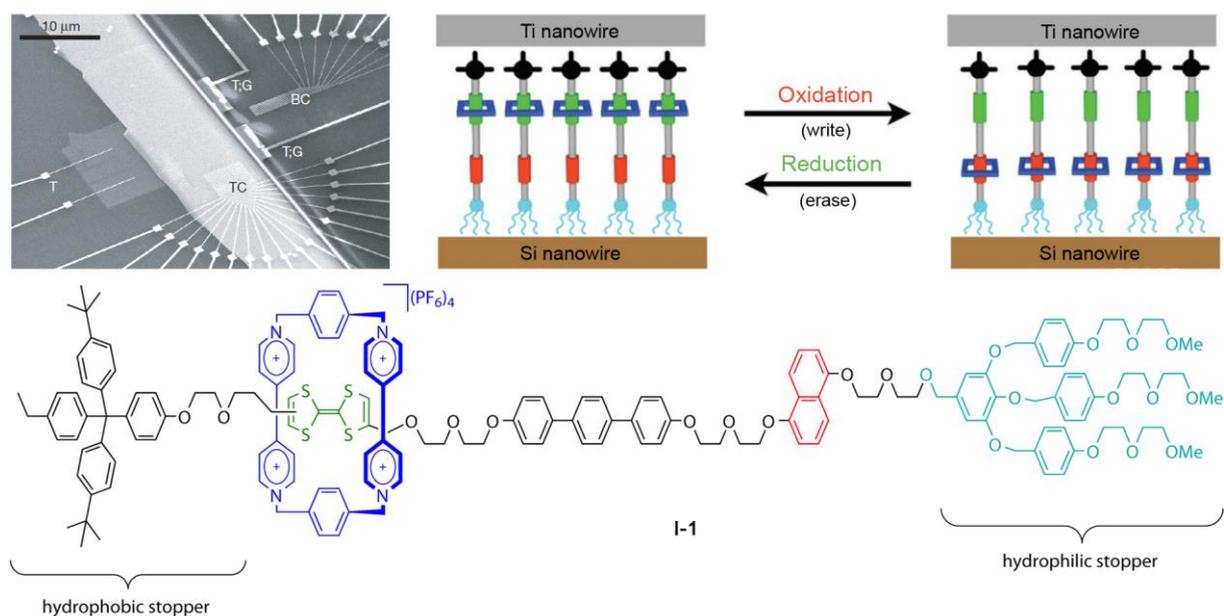
Figure 1. Top left: Electron microscopic image of a nanowire crossbar memory. The array of 400 Si bottom nanowires extends diagonally up from bottom left. The top array of 400 Ti nanowires is covered by a template of 400 Pt nanowires, and extends diagonally down from top left (T = testing contacts, G = grounding contacts, TC =top contacts, BC =bottom contacts). Reprinted with permission from Ref. [4]. Copyright 2007 Nature Publishing Group. Top right: Schematic representation of the write/erase sequence *via* redox cycling of the green TTF unit (see chapter 1.2.2). Reproduced from Ref. [5]. Bottom: The electronically switchable molecule **I-1** that was incorporated in the device.[4]

Even if the array features a significant number of defects, the working bits could be identified, isolated and configured to form a fully functional random access memory circuit for storing and retrieving information. This unique architecture undoubtedly proves that many of the most challenging scientific issues associated with integrating nanowires, molecular materials, and defect-tolerant circuit architectures at extreme dimensions are solvable. These results provide a compelling demonstration of many nanotechnological concepts that were introduced by the Teramac supercomputer featuring a defect-tolerant architecture several years before.[6] Thus, this single example beautifully demonstrates how engineering, information technology, physics and chemistry cooperate and exceed the boundaries of what is possible in terms of miniaturizing functional elements. This will certainly be one of the main endeavors of future nanoscientists to further elaborate this prolific symbiosis and construct functional machines on the molecular scale.

1.2   Supramolecular Chemistry

Historically, chemists' understanding of nature was based on an entirely molecular perspective, where structures, properties and functions originate from strong covalent bonds. It took a long time to comprehend that crucial biological processes do not rely on the formation or breaking of such bonds. After Emil Fischer first proposed the lock and key model in 1894 to describe enzyme-substrate interactions,[7] a new concept gradually evolved within the field. Subsequent generations of scientists found that biological structures commonly consist of loose assemblies held together by weak, non-covalent forces. It is for their dynamic character that these interactions are essential for a plethora of processes taking place in living organisms. Fischer's description of enzymes' mechanism of action ultimately entailed two pioneering principles: Molecular recognition and supramolecular function. These two concepts soon developed into a new subject, namely supramolecular chemistry.

The term was coined in the late 1960s by Jean-Marie Lehn during his studies of inclusion compounds and cryptands.[8] His definition of the subject is as simple as it is astonishing: "Chemistry beyond the molecule" or "chemistry of the intermolecular bond."[9] The ground breaking development and use of molecules with structure-specific interactions of high selectivity was awarded with the Nobel Prize in 1987 for Charles Pedersen, Donald J. Cram, and Jean-Marie Lehn and thus, supramolecular chemistry was fully recognized as a mature chemical discipline.[10] Three of said molecules are shown in Figure 2, namely the crown ether **I-2**, the cryptand **I-3**, and the spherand **I-4**.[8,11]

crown ether **(I-2)**   cryptand **(I-3)**   spherand **(I-4)**
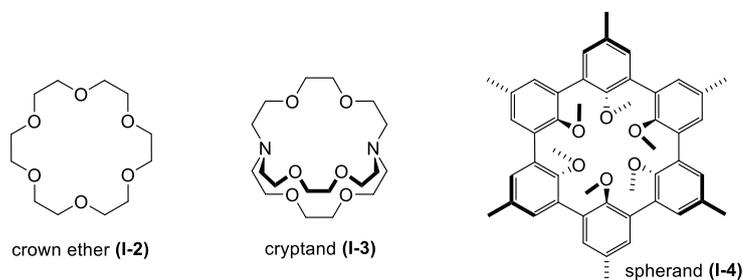
Figure 2.   Early supramolecular cation binders: Crown ether **I-2**, cryptand **I-3**, and spherand **I-4**.[8,11]

Nature itself serves as an inexhaustible source of inspiration for supramolecular chemists. Without highly precise and specific intermolecular interactions, life as we know it would never have had a change to evolve to its present state. Incredibly complex in some ways, elegantly simple in some others, nature evolved a manifold chemistry of hierarchy, selectivity, cooperation and specificity laying the foundation stone for living organisms interacting with and proliferating in their given environment.[12] In supramolecular terms, biochemical hosts are receptors of enzymes, antibodies, ionophores, or genes. Their interacting counterparts are amongst others substrates, inhibitors, co-factors, drugs, or antigens. All of these components feature supramolecular properties in various modes, such as self-organization, self-assembly, self-replication, molecular recognition, or kinetic and thermodynamic complementarity. The basis of virtually all these characteristics are supramolecular interactions of different kinds, for example ion-dipole

interactions, hydrogen bonding, π-interactions with cations, anions, and other π-systems, van der Waals forces, or closed shell interactions (for example aurophilic interactions, halogen bonding).[12]
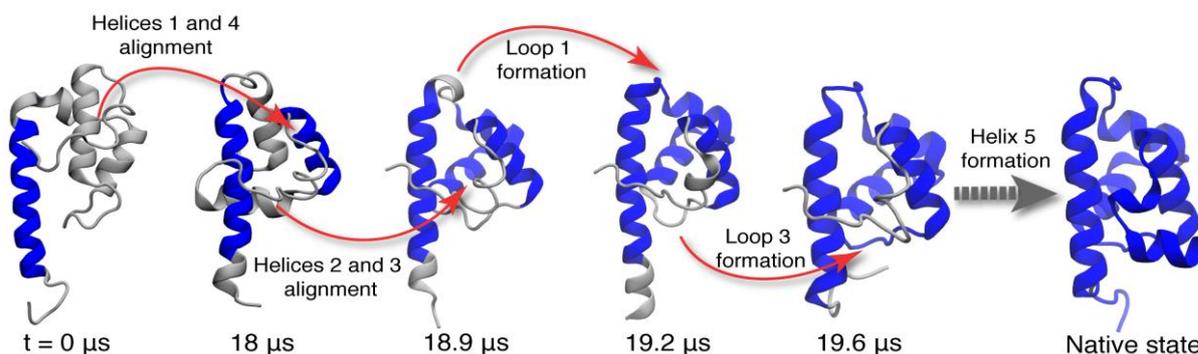
Scheme 1.   Protein folding as an example for a process governed and directed by supramolecular interactions. Reprinted with permission from Ref. [13]. Copyright 2007 American Chemical Society.

Modern supramolecular chemistry as a scientific discipline aims at designing functional assemblies based on multiple molecular components held together by non-covalent, intermolecular forces. It has become a versatile and competitive field of research during the last decades and has fueled numerous developments at the interfaces with other science branches, such as biology, physics and engineering. In the following sections, some of the underlying concepts will be explained and key compounds in this field of research discussed in greater detail.

1.2.1   Host-Guest Interactions & Anion Recognition

The central motif of supramolecular functionality is certainly that of host-guest interactions. In its simplest sense a molecule, the "host", binds another molecule, the "guest" to form a host-guest complex, also referred to as supermolecule.[14] In general, the host systems consist of larger molecules or assemblies, such as macrocyclic scaffolds with suitable functional groups, or proteins exhibiting accessible cavities. The guest can be a monoatomic cation, a simple inorganic anion, a small organic entity but also a sophisticated molecule, such as a hormone, or a pheromone.
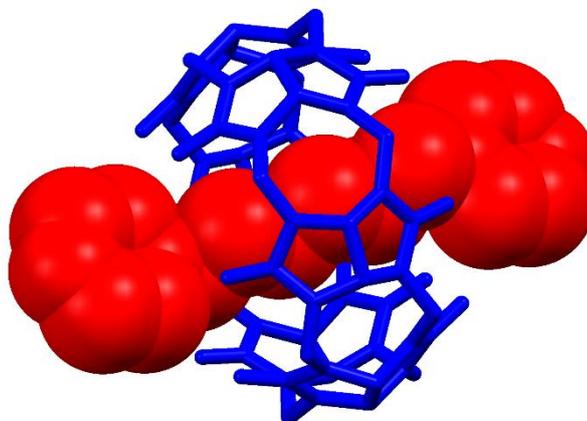
Figure 3.   Crystal structure of a host-guest complex with a 1,6-dipyrazinium-substituted hexane entity (shown in red as space filling model) bound within a cucurbit[6]uril host (shown in blue as capped sticks). Content reproduced from Ref. [15].

From a more formal perspective, the host comprises convergent binding sites, such as Lewis basic, or hydrogen bond donors, the guest in turn possesses divergent binding sites, for example Lewis acidic metal cations, or hydrogen bond accepting functionalities.[16] Thus, host-guest complexes are generally held together by comparably weak non-covalent interactions, such as hydrogen bonding, ion pairing, π–π stacking, or van der Waals interactions.[17] Figure 3 depicts an example of a host-guest complex, more specifically a pseudorotaxane that is held together by said weak interactions. Supramolecular assemblies of this kind belong to a subgroup of host-guest complexes where both the host and guest are organic or hybrid organic-inorganic molecules. More specifically, the hosting compound is generally a so-called cavitand, a molecule that features a permanent and intrinsic cavity suitable for guest-binding.[12] Consequently, the guest entity has to be of geometrical dimensions that allow for entering or even penetration of the cavity. A supramolecular complex forms in the case the interactions between both components are thermodynamically favorable over the situation where they are separated. This usually implies that the host and guest contain functionalities that render their association advantageous. The resulting interactions can be weak (e.g. van der Waals, or hydrophobic/solvophobic interactions), but also comparatively strong (e. g. hydrogen bonds, or Coulomb interactions). Arguably one of the most important features of cavitands is their specific shape. Virtually all cavitands' structures exhibit an intrinsic curvature, leading to a container-like shape with an enforced concavity.[12] Figure 4 shows some examples of host compounds that have been extensively employed for guest binding in solution and Table 1 lists some of their geometrical properties.
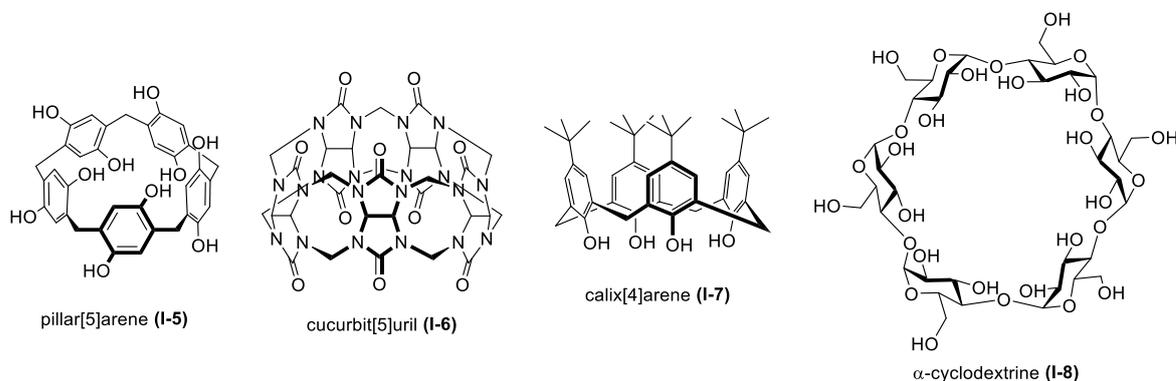
Figure 4.   Frequently employed organic host systems pillar[5]arene (**I-5**), cucurbit[5]uril (**I-6**), calix[4]arene (**I-7**), and α-cyclodextrine (**I-8**).[18]

The relatively young family of pillar[*n*]arenes, such as **I-5**, have an ever increasing impact on host-guest chemistry since their first synthesis in 2008 by Ogoshi and co-workers.[18d] They consist of hydrochinone units (5 to 15) that are linked *via* methylene bridges in *para*-position to each other. They can be synthesized *via* a straightforward one-pot reaction between 1,4-dimethoxybenzene and paraformaldehyde in the presence of a Lewis acid. The methoxy groups are subsequently cleaved off with boron tribromide to yield the pillar[5]arene. Higher pillar[*n*]arenes are accessible by template approaches (for *n* = 6),[19] or a by ring expansion of pillar[5]arene (for *n* = 6-15).[20] They exhibit a very symmetrical cylindrical cavity in contrast to the cone-like structures of many other supramolecular hosts.[21] A related family of organic host compounds is the class of cucurbit[*n*]urils (**I-6**, from Latin *cucurbita* = pumpkin) consisting of several CH$_2$-bridged glycoluril units. They were first synthesized in 1905,[22] however, not structurally characterized until 1981.[23] To date, homologues consisting of 5 to 10 repeating units have been characterized. They are synthetically

accessible by condensation reactions of urea and an α-dicarbonyl compound, such as glyoxal. The intermediary glycoluril is then condensed with formaldehyde to yield the respective macrocycles.[18c] Their pumpkin-like shape leads to the particularity that the cavity is of a larger size than the portals at both ends of the structure. This causes a different size selectivity of cucurbit[n]urils compared to host-compounds with comparable cavity dimensions.[24]

Table 1. Comparison of the cavity properties of different organic host compounds.

	I-5[21]	**I-6**[24]	**I-7**[25]	**I-8**[26]	cucurbit[6]uril[24]
shape	cylinder	pumpkin	basket	bucket	pumpkin
inner diameter (Å)	5.5	4.4 (portal: 2.4)	≈ 5	4.7	5.8 (portal: 3.9)
height (Å)	7.8	9.1	6.0	7.9	9.1

Another widely employed group of cyclophanes are the calix[n]arenes (from Latin *calix* = chalice), the hydroxyalkylation products of phenols and aldehydes. Similar to the cucurbit[n]urils they have been synthesized early on in 1872,[27] but not structurally recognized until 1979.[28] Calix[n]arenes generally adopt a cone-shaped structure as shown for **I-7** (Figure 4), however, their conformation is in dynamic equilibrium with three other modes, namely partial cone, 1,3-alternate, and 1,2-alternate.[29] The desired cone conformation can be locked by exchanging the hydroxyl groups with bulkier substituents to increase the rotational barrier. Alternatively, placing a sterically demanding group on the upper rim likewise prevents rotation.[18a] A somewhat special class are the cyclodextrins, such as **I-8** (Figure 4), as they are not accessible by classical synthetic chemistry, but instead are selectively produced by enzymes (cyclodextrin glycosyltransferases) during the breakdown of starch.[30] Accordingly, they consist of glucose molecules that are 1,4-glycosidically linked to each other to form macrocycles with at least six ring members. A Greek letter is used as a prefix to define the number of glucose units with α = 6, β = 7 *etc*.[18b] Cyclodextrins exhibit a hydrophobic cavity with a very polar outer surface and thus are capable to form host-guest complexes with apolar organic molecules in highly polar solvents.

Apart from these frequently encountered organic host complexes a huge variety of further organic scaffolds for this purpose has been developed.[12] Additionally, more recent research interests seek to include metal ions into so-called metallocavitands to allow for a broader spectrum of structural motifs or functionality, such as catalytic or sensing capabilities.[31] This type of supramolecular chemistry where the guest entities are themselves either simple or highly complex organic molecules will certainly play a crucial future role for the development of sophisticated assemblies, for example for smart drugs, or molecular machines.[32]

A further major subcategory of supramolecular chemistry is focused on the recognition of anions by tailored receptors. It has developed from its beginnings in the late 1960s with positively charged ammonium cryptands, such as **I-9** (Figure 5) for halide binding to a manifold of charged and neutral, cyclic and acyclic, inorganic and organic supramolecular host architectures for the selective complexation, detection, and separation of anionic guest entities.[33] This area of research is of immense universal interest, as anions not only are ubiquitous in biological systems (polyanionic DNA, numerous enzyme substrates and co-factors), but also play adverse roles in medicine (carcinogenesis related to metabolites of nitrate),[34] or environmental science (river

eutrophication caused by phosphate-based fertilizers).[35] Designing anions receptors is in general more challenging than analogues for cation recognition due to the fact that anions have a lower charge to radius ratio, oftentimes exhibit sensitivity towards pH changes and have a wide range of geometries ranging from spherical to highly complex.[33] Thus, for the design of effective receptors several factors have to be taken into account, such as geometry or basicity of the respective anion, as well as solvent effects. It proved useful to sort the manifold of different receptors into categories based on the type of their interaction responsible for guest complexation, for example electrostatic or hydrogen bonding interactions (**I-9**, **I-10**, Figure 5), metal or Lewis acid coordination (**I-12**, Figure 5), or complexation caused by the hydrophobic effect. For some compounds a clear-cut classification into one specific group is not possible, as more than one interaction motifs can be implemented simultaneously, as is the case for **I-11**, where an ensemble of hydrogen bonding, Coulomb interaction, as well as π–π stacking contribute to the overall receptor properties.[36]
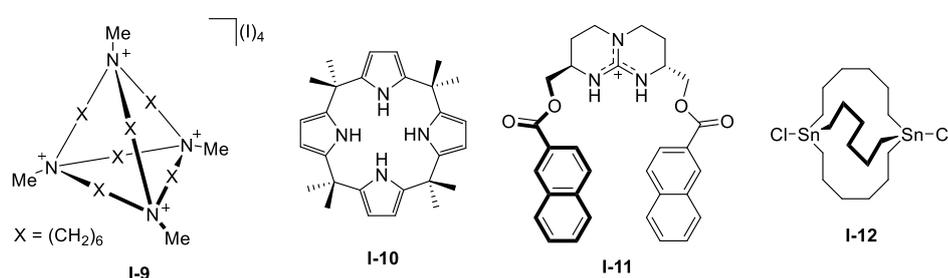
Figure 5.   Examples for anion receptors based on different binding strategies: electrostatic interaction (**I-9**),[37] hydrogen bonding (**I-10**),[38] a combination of both (**I-11**, additional π–π stacking interaction possible),[36] and Lewis acid coordination (**I-12**).[39]

An even more sophisticated research focus based on this receptor chemistry is the implementation of functionality in the host molecules in a way that they are able to selectively bind and sense the anion recognition event through a macroscopic, electrochemical, or optical response.[40] In terms of electrochemical detection the most straightforward approach is the generation of a current/potential perturbation of a redox-active host upon complex formation.[41] Optical sensing on the other hand relies on the high sensitivity of fluorescent techniques for assessing target guest species, commonly achieved by covalent attachment of organic and inorganic luminophores in proximity to charged guest-recognition sites.[42] In contrast, the great benefit of colorimetric sensors over both electrochemical and optical methods is the fact that usually no technical device is necessary to detect the supramolecular complexation, because the binding event in these systems is accompanied by a macroscopically visible color change. Exemplarily, Sessler *et al.* reported a sensor based on a 2,3-dipyrrol-2'-ylquinoxaline-scaffold that allows for the detection of fluoride ions in solution *via* an observable color change from yellow to purple upon host-guest interaction.[43] This effect is highly dependent on fluoride and was not identified with other anions.

During the last decade host-guest chemistry involving both neutral and anionic guest compounds, has a made significant progress from a predominantly academic reign to demonstrable applications.[40] Certainly, this trend will continue, rendering supramolecular assemblies highly interesting research targets with immense future potential.

1.2.2   The Mechanical Bond & Molecular Machines

When Linus Pauling's "The Nature of the Chemical Bond" – one of the most significant chemistry books ever written – was published in 1939 as a summary of the pioneering work that had been carried out in the 1920s and 1930s,[44] chemical bonding was classified into the three classic categories that still hold true in the present days: Electrostatic, covalent and metallic bonds as extremes between which a variety of intermediate bonding motifs exist. Roughly 20 years later a new type of bond surfaced that contradicted this paradigm, namely the mechanical bond which might be defined as an entanglement in space between two or more molecular entities (component parts) such that they cannot be separated without breaking or distorting chemical bonds between atoms.[45] In contrast to classical chemical bonds that are typically located between proximal atoms, mechanical bonds are shared between groups of atoms or molecular moieties.

Within the field of mechanomolecules the two key structural motifs are without doubt the archetypical interlocked scaffolds – rotaxanes and catenanes. A rotaxane (from Latin *rota* = wheel and *axis* = axle) consists of a ring component that is threaded by an axle-like moiety, the 'dumbbell', with sterically demanding endgroups ('stoppers') preventing transgression (Figure 6, left).[46] In contrast, a catenane (from Latin *catena* = chain) comprises two or more interlocking, ring-shaped molecular entities (Figure 6, middle).[47]
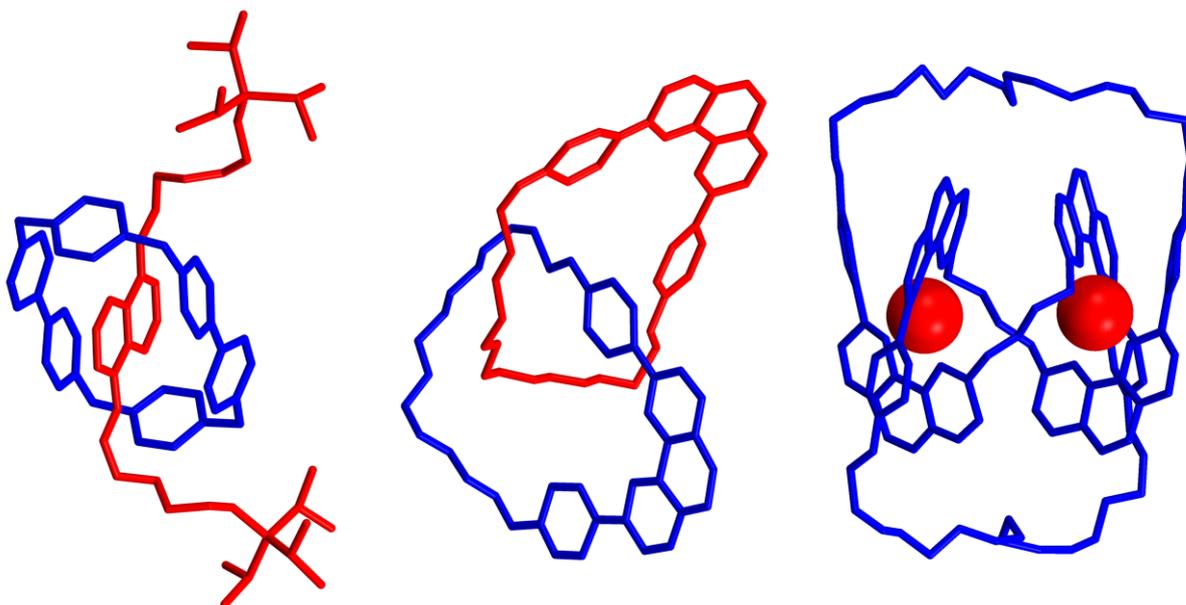
Figure 6.   Molecular structures of a [2]rotaxane (left), a [2]catenane (middle), and a trefoil knot (right) shown in capped sticks (metal atoms in space filling representation). Hydrogen atoms, counter ions and co-crystallized solvent molecules have been omitted for clarity. Content reproduced from Ref. [48], [49] and [50].

The chemistry of mechanomolecules is situated within several intersecting chemical disciplines, namely supramolecular chemistry, mechanostereochemistry, and chemical topology (Figure 7). Both rotaxanes and catenanes belong to the area of compounds referred to as mechanically locked molecules (MIMs).[5,51] A mechanical bond is not a necessary prerequisite for these interlocked architectures, since also entanglements can occur in molecules that do not contain

distinguishable components, such as molecular knots (Figure 6, right). A closely related field is that of chemical topology.[52] It consists of molecules whose graph (i.e. their representation based on atoms and bonds) is nonplanar implying that it cannot be represented in a single plane without crossing points. In a topologic sense, the object can be distorted to any extent, but its topological properties are unaltered given that no cleavage occurs.[53] Some types of MIMs are considered chemical topologies, such as catenanes or knots, whereas rotaxanes and similar assemblies are per definition topologically trivial, as their components are separable upon continuous deformation. On the other side, mechanically interlocked architectures are generally not identified as supermolecules, because their constituents are not able to dissociate and exchange, in case the mechanical bond is maintained by durable covalent bonds. The boundary between mechanomolecules and supermolecules for compounds that lack sufficiently bulky stoppers preventing a dethreading of the axle part, so-called pseudorotaxanes,[54] is not conclusively defined and thus blurry.
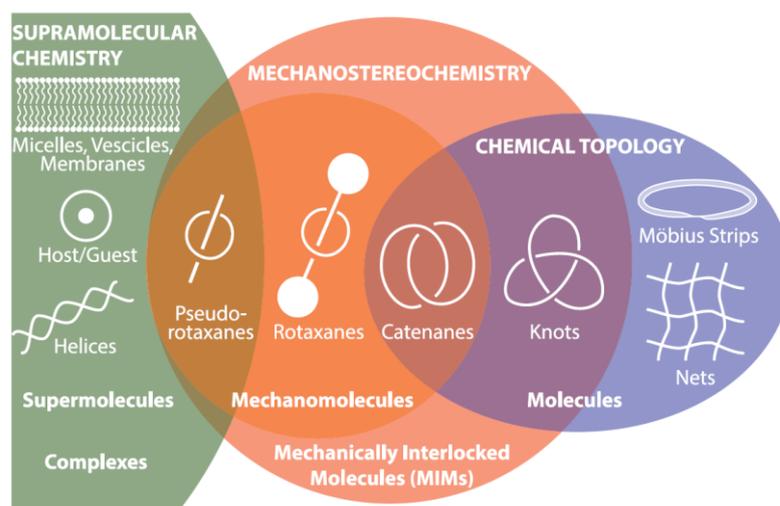
Figure 7.   Different types of molecular species fit into the intersecting fields of supramolecular chemistry, mechanostereochemistry, and chemical topology illustrated by a Venn diagram. Reprinted with permission from Ref. [45]. Copyright 2017 John Wiley & Sons.

Whether a mechanical bond can be considered a chemical bond is not to be answered in an entirely conclusive manner. When projecting Pauling's definition of a chemical bond onto the situation encountered in mechanically interlocked molecules, it shows that all criteria are fulfilled. The same holds true for the IUPAC Gold Book definition,[55] which is a strong argument in its favor. However, mechanical bonds are a grey area in terms of chemical bonding due to the fact that they are considered to be stable bonds in molecules, yet maintained exclusively by the physical forces that prevent a detangling of the involved components. In turn, this means that unlike chemical bonds there are no enthalpic gains or losses associated with breaking or making mechanical bonds, suggesting that its strength is in the range of the weakest chemical bond maintaining it.

The question of how to synthetically make such mechanical bonds was first discussed as early as 1915,[47] however, the first [2]catenane for which evidence was put forward in support of its structure was reported by Wasserman in 1960 – in a yield of approximately 0.0001 % as indicated by IR spectroscopy.[56] The early statistical and directed synthetic approaches to mechanically

interlocked molecules that followed in subsequent years suffered from either low yields, lengthy synthetic procedures, or both.[57] The break-through that was responsible for overcoming these drawbacks was the application of passive template synthesis to the preparation of entwined and interlocked structures, first reported by Sauvage *et al.* in 1983.[58] A hydroxy-functionalized 2,9-diphenyl-1,10-phenanthroline ligand **I-14** and the related macrocycle **I-13** adopt a threaded structure (**I-15**) upon coordinating a Cu^I ion in tetrahedral fashion (Scheme 2).
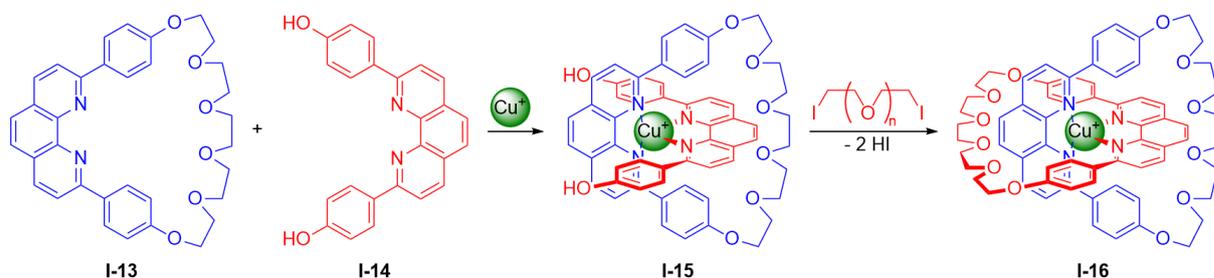
Scheme 2.　　Passive template synthesis of [2]catenane **I-16** by Sauvage and co-workers.[49]

The perpendicular ligand arrangement generates a crossing point between **I-13** and **I-14**. Thus, a subsequent ring closure by a Williamson ether macrocyclization reaction conveniently resulted in the [2]catenane **I-16** in 42% yield. The copper ion could be removed quantitatively from **I-16** through addition of potassium cyanide to afford the metal-free analogue. Apart from high yields and reduced synthetic efforts, Sauvage's method allowed for predictability and reliability in template preorganization enabling the rational design of synthetic pathways to more complex topologies. Over the past three decades these have enabled a plethora of mesmerizing mechanically interlocked molecular architectures of ever increasing complexity. Their complete treatment would certainly go beyond the scope of the introduction, however, several review articles are available covering this persistently growing field of research.[47,52e,52h,53]

As mentioned above, the second major class of molecular interlocked molecules is that of rotaxane scaffolds. The first example of such an architecture was synthesized in 1967 by Schill *et al.* *via* a multistep synthesis,[59] and by Harrison *et al.* making use of a statistical approach.[60] However, these early synthetic efforts suffered from the same problem as described for the first catenane systems, namely low yields and cumbersome procedures. Only after template-supported strategies for the synthesis of catenanes were developed, the related rotaxanes became likewise accessible on a preparative scale.
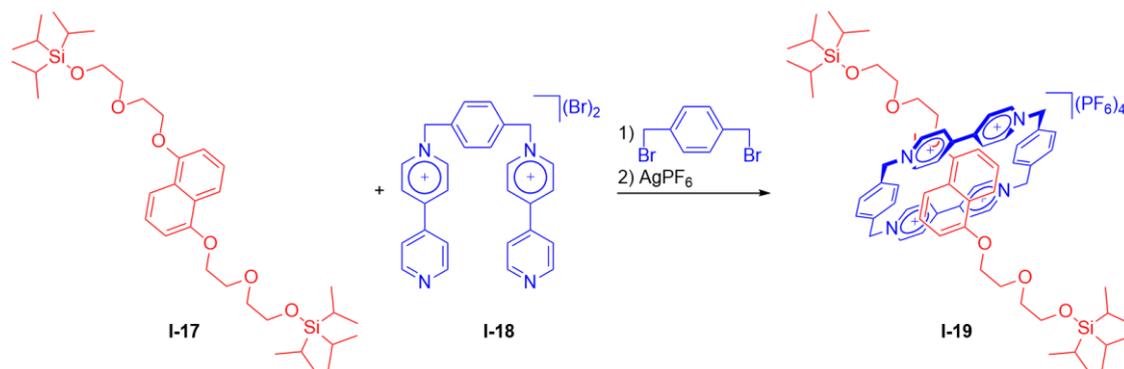
Scheme 3.　　High-yielding synthetic approach for pyridinium-based [2]rotaxane by Stoddart and co-workers.[48]

Stoddart *et al.* found that for the rotaxane synthesis a charged template approach initially developed for catenanes is highly beneficial.[61] Exemplarily, they synthesized the rotaxane **I-19** (Scheme 3) by taking advantage of strong binding affinities between the π-electron-deficient dicationic di(pyridinium) salt **I-18** and the π-electron-rich aryl ether **I-17** with bulky triisopropylsilyl ether substituents.[48] The two starting materials have a high tendency for π–π stacking interactions and thus, 1,4-di(bromomethyl)benzene can be added to introduce a macrocyclization reaction affording cyclobis(paraquat-*p*-phenylene) (CBPQT^{4+}) threaded on the axle entity. In the last two decades a spectrum of further synthetic approaches for rotaxanes has been developed, such as capping,[62] slipping,[63] or snapping.[64] These methods are not covered in this short introduction, but are subject to numerous review articles.[46,51c,65]

The central question of this chemistry that has arisen with the successful syntheses of such interlocked structures is whether they can be employed in machine-like applications on a molecular level. As is often the case in chemistry, Mother Nature provides inspiration by operating highly complex protein-based machines that became essential to virtually all living organisms. One of the most elegant molecular devices omnipresent in cells is certainly the ATP synthase (Figure 8).[66] This protein complex couples the enthalpy of a proton transfer along a concentration gradient over a membrane with the generation of ATP, the cellular energy equivalents. The ATP synthase consists of two functional subunits F_o and F_1, that are associated with each other within the membrane, but not chemically bonded.[67] The F_o unit contains a transmembrane proton channel and forms a rotor that is powered by the flow of protons through it. This rotor moves within a complex of the catalytically active subunit of the static F_1 component and thereby causes a conformational change within the F_1 unit, which enables the synthesis of ATP from ADP and inorganic phosphate.
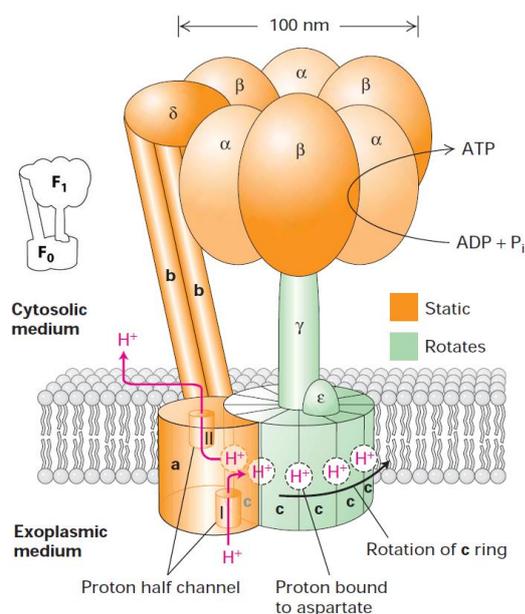
Figure 8. Model of the structure and function of ATP synthase (the F_oF_1 complex) in the bacterial plasma membrane. Reprinted with permission from Ref. [68]. Copyright 2007 W. H. Freeman & Company.

The structural properties of the ATP synthase, before all the rotating rod within a static component, is closely related to those of rotaxanes, thus rendering this class of molecular interlocked molecules as potential, highly simplified model systems for machine-like behavior on a

molecular level.[69] One of the prevalent challenges for the design of molecular machines is the fact that molecules are in constant motion, driven by the kinetic energy of the molecules surrounding them. This phenomenon is referred to as Brownian motion and needs to be overcome in order to generate machine-like precision and function. Mechanomolecules are intrinsically equipped with this potential as the mechanical bond allows components to move along certain pathways while restricting motion along other routes.[65] A central concept in this context is that of multistability meaning that a molecule features several (co-)conformations that represent energetic minima.[70] In the case of a bistable MIM, the global energetic minimum is generally referred to as the ground-state co-conformation (GSCC, Scheme 4) and any higher-energy minimum, a metastable state co-conformation (MSCC, Scheme 4).[71] Controlled switching based on co-conformational transformations usually is initiated by applying an external stimulus causing a change of the magnitude of $\Delta G°$ by raising or lowering the stability of one or more translational isomers, which in turn modulates $\Delta G^{\ddagger}$ as a consequence. A schematic example of this approach is shown in Scheme 4. An external stimulus disfavors the noncovalent bonding interactions in the GSCC of a bistable rotaxane leading to the population of the secondary binding site. Upon reversion of the stimulus the system gradually relaxes back to the GSCC depending on the height of energetic barrier between both states.[71]
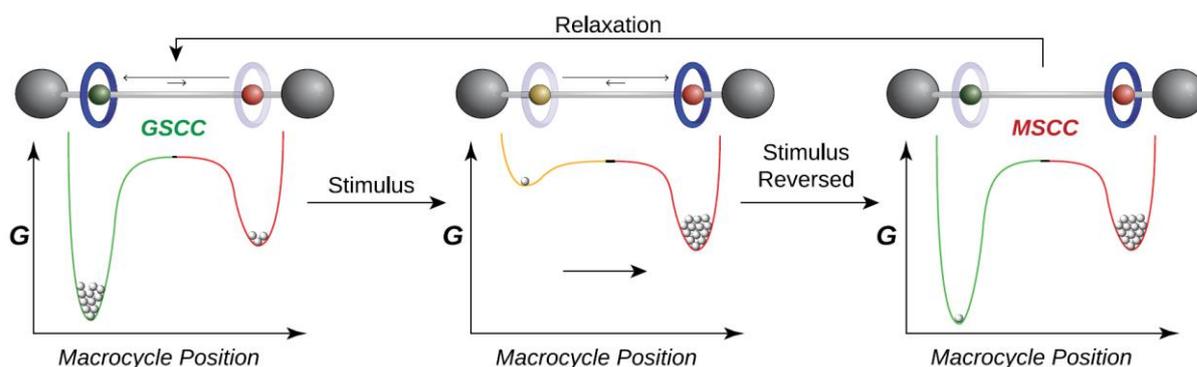
Scheme 4.   Switching-mechanism in mechanically interlocked molecules, exemplified by the potential energy surface diagram of a bistable [2]rotaxane (GSCC = ground state co-conformation, MSCC = metastable co-conformation). Reprinted with permission from Ref. [45]. Copyright 2017 John Wiley & Sons.

The external stimulus that induces the switching motion can be of manifold origin. The most straightforward method is a physical excitation, amongst others heat (higher temperatures favor entropically governed processes, such as increased ring mobility, over enthalpically governed processes, such as non-covalent interactions), light (including photoinduced electron transfer processes), pressure, or solvent polarity. Alternatively, chemical stimuli can be employed, for example pH changes, variations of oxidation states by redox processes, or influencing the coordination numbers and geometries of ligated metal ions. A third option is an electrochemical manipulation of interactions like electrostatic and hydrogen bonding, or π–π stacking.

One example for a redox-switchable molecular architecture is the [2]catenane **[I-20]**[4+], reported by Stoddart *et al.* in 1998 (Scheme 5).[72] It consists of the cyclobis(paraquat-*p*-phenylen) entity that is interlocked with a macrocycle containing the easily and reversibly oxidized compound tetrathiafulvalene (TTF),[73] which interacts strongly with CBPQT[4+] in the reduced state.[74] The second functional group in this ring is the relatively redox-inactive donor site 1,5-dioxynaphthalene

(DNP) that binds the CBPQT[4+] ring much more weakly. In its GSCC, the TTF unit is encircled by the CBPQT[4+] ring. Two one-electron oxidations of TTF yield the hexacationic **[I-20]⁶⁺** species in which the TTF²⁺ dication is ejected from the ring due to Coulombic repulsion. Reduction of TTF²⁺ back to TTF populates the MSCC of **[I-20]⁴⁺** before the GSCC is gradually recovered.[72]
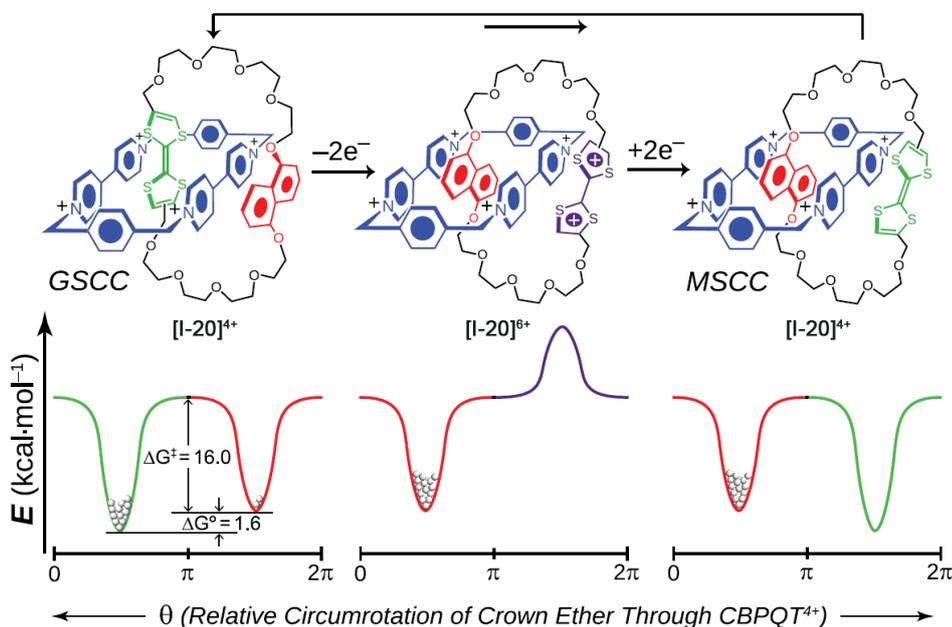
Scheme 5. Bistable [2]catenane **[I-20]⁴⁺**, its electrochemical oxidation to **[I-20]⁶⁺** and subsequent reversal of the redox stimulus leading to a population of the MSCC of **[I-20]⁴⁺**, which then relaxes back to the GSCC. Reprinted and modified with permission from Ref. [45]. Copyright 2017 John Wiley & Sons.

These relatively simple functional molecules were the origin for the development of highly sophisticated machine-like assemblies. Exemplarily, Leigh and co-workers presented architectures that are able to act as sequence-specific peptide synthesizer,[75] or function as autonomous chemically fueled small-molecule motor that shows unidirectional movement,[76] one of the most difficult tasks within this field. Another very successful approach for the synthesis of molecular machines was developed by the group of Feringa relying on chiral overcrowded alkenes that can be reversibly photoisomerized leading to unidirectional rotation about the central double bond.[77] The Nobel Prize in chemistry 2016 was awarded jointly to Jean-Pierre Sauvage, Sir J. Fraser Stoddart and Bernard L. Feringa for their efforts towards the design and synthesis of molecular machines.[78]

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2 THE CHEMISTRY OF *N*-HETEROCYCLIC CARBENES

This chapter intends to give a comprehensive introduction to *N*-heterocyclic carbenes and their impact on modern chemistry. It presents synthetic routes for NHC ligand precursors and complexes, their electronic and steric properties, as well as fine-tuning possibilities for both. Additionally, macrocyclic and pyrazole-bridged NHC compounds and their unique properties will be discussed, in order to provide a contextual basis for the scientific results presented in this work. Finally, a brief section will be dedicated to the most prominent applications of NHC complexes.

2.1   General Remarks

"From laboratory curiosities to efficient synthetic tools"[1] – This is arguably the best way to describe the rise of *N*-heterocyclic carbenes as powerful ligand systems for metal ions throughout the periodic table. The first report of NHC complexes goes back almost 50 years to the year 1968, when Öfele and Wanzlick *et al.* independently synthesized a chromium and a mercury complex, respectively.[2] Outright after their discovery this chemistry fell into a deep sleep that lasted over two decades. Only seldom reports by Lappert *et al.* surfaced describing heterocyclic carbene compounds derived from electron-rich tetraamines.[3] The perception of NHCs radically changed when the groups of Bertrand and Arduengo reported the first examples of isolable free carbenes.[4] Formerly believed to be intangible, intermediary species they turned out be stable, yet powerful synthons that can readily be stored and handled. The field then got jump-started in the mid-1990s when Herrmann *et al.* introduced NHCs as spectator ligands to homogeneous catalysis (Figure 9).[5]
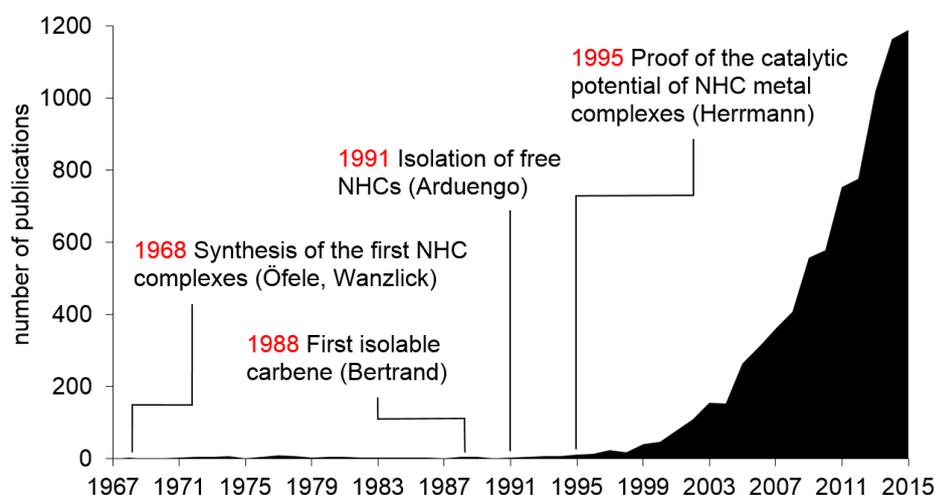
Figure 9.   Graphical representation of the entries for "*N*-heterocyclic carbene" in SciFinder (journals, reviews and patents as of 06.10.2017) including the milestones of the NHC development.[2b,4,5b,6]

Within only a few years from then a plethora of publications[7] reporting novel synthetic procedures for NHC compounds,[8] and their utilization in homogeneous catalysis,[9] but also as fine-tuned materials for a huge variety of applications beyond catalysis.[10] This enormous boost in importance certainly derives from the unique and unprecedented properties of this class of carbenes, such as their high stability, a wide range of easily tunable electron donor strength, as well as a great variability of steric demand. These characteristics rendered them not only equally well applicable, but oftentimes superior compared to state-of-the-art phosphines.[11]

By definition *N*-heterocyclic carbenes' structural basis can be any nitrogen-containing heterocyclic scaffold, however, the by far most applied building units are based on imidazole and its hydrogenated congener imidazoline. Other entities, such as pyrazoles,[12] 1,2,3-triazoles,[13] 1,2,4-triazoles,[14] or tetrazoles[15] have been employed in a similar fashion, but are far less researched (Table 2). Importantly, not only the number and relative position of the nitrogen atoms in the heterocycle are subject to variation, but also the substitution pattern of the ring-atoms leading to a change in position of the carbene carbon atom in the system. Therefrom, compounds are formed that do not exhibit a mesomeric structure without zwitterionic character, so-called abnormal or mesoionic NHCs (aNHCs, MICs). The abnormal pyrazole-type carbene **I-22a** features another particularity, namely the fact that the stabilizing heteroatoms are located in more distant positions, leading to so-called remote carbenes (rNHCs). Another exciting property of some NHC ligands is their capability to combine both normal and abnormal binding and thus are able to coordinate two metal centers at once resulting in *N*-heterocyclic di(carbenes) (NHDCs).[16]

Table 2. Selection of normal and abnormal NHCs based on exclusively nitrogen-containing five-membered heterocycles. The abnormal pyrazolylidene **I-22a** is in addition an example for a remote carbene.

Apart from these five-membered azolylidene systems a multitude of ring modifications have been achieved over the last decades. The ring atoms are by no means restricted to carbon and nitrogen and consequently examples containing other heteroatoms, such as oxygen, silicon, phosphorus, boron, or sulphur have been reported.[17] Likewise, the ring size of the heterocycle can be modified. Next to the ubiquitous five-membered rings, systems containing four, six and seven atoms have been synthesized.[17b] A huge number of further modifications of the heterocycle, the substituents, or a combination of both, led to immense plurality of *N*-heterocyclic carbene scaffolds with a manifold of different characteristics (Figure 10).
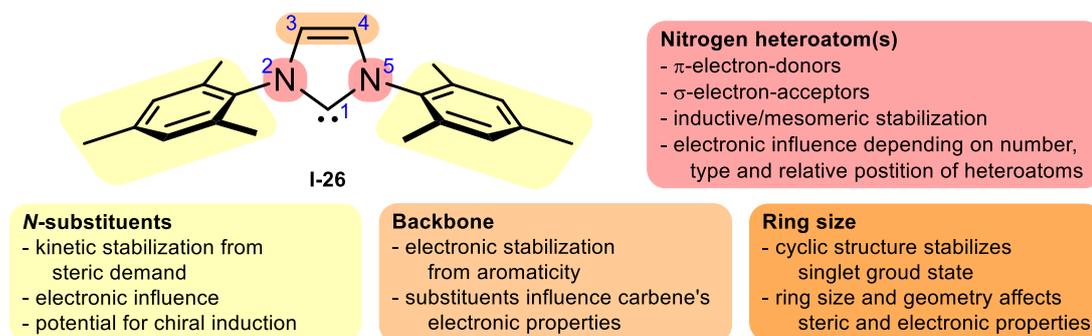

Figure 10. Structural properties of *N*-heterocyclic carbenes, exemplarily demonstrated with di(mesityl)-imidazolylidene **I-26**.[8e] The general numbering scheme is illustrated by blue numbers.

2.2 Synthetic Approaches towards NHC complexes

Over the past decades a plethora of synthetic routes towards NHC ligand precursors and complexes have been discovered.[8b,18] Their complete account certainly goes beyond the scope of this comprehensive introduction. Hence, the following paragraphs are confined to the most commonly encountered synthesic routes in this field. For a more in-depth overview a variety of review articles covering this topic is available.[8b,8d,8e,9a,9d,18-19] As this work exclusively deals with imidazole-based carbenes, the chemistry related to these heterocycles will be in the focus.

2.2.1 Synthetic Routes to NHC Ligand Precursors

By far the most common precursors for NHC complexes of any kind are azolium salts that are transformed to the carbene ligand after C–H deprotonation of the C2 carbon atom. For the synthesis of NHC ligand precursors a multitude of synthetic approaches have been developed, also due to the fact that systems with sterically demanding substituents are generally not feasible *via* standard substitution reactions.[18] Especially for wingtips with bulky groups in *ortho*-positions early approaches did not yield any, or only minimal amounts of product.[20] Subsequently, a ring-closing procedure *via* introduction of the backbone as the final step allowing for a straightforward accessibility of imidazolium salts with a symmetrical wingtip pattern was developed by Nolan *et al.* (Scheme 6, top).[21] As starting materials simple, in most cases commercially available aromatic or aliphatic amines are employed that are reacted with glyoxal to give the respective diimine as the condensation product. In a subsequent cyclization step with paraformaldehyde and hydrochloric acid the desired imidazolium chloride, such as **I-27** is obtained in high yields.[22] A related protocol for the synthesis of sterically congested imidazolium salts was reported by Arduengo *et al.* relying on the reagent chloromethylethyl ether for the ring closing reaction.[23] The disadvantage of these two methods, however, is the fact that only symmetrical imidazolium salts are accessible.
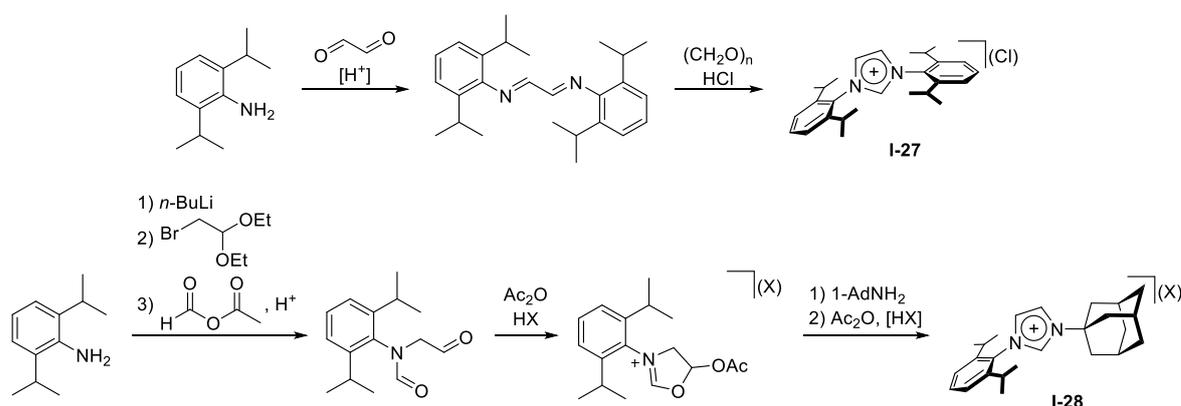
Scheme 6.   Synthetic routes towards sterically demanding diaryl-substituted NHC ligand precursors. Top: symmetrical imidazolium salt **I-27** *via* glyoxal condensation.[21a] Bottom: unsymmetrical imidazolium salt **I-28** *via* heterocycle-interconversion.[24]

For the synthesis of unsymmetrical imidazolium precursors, such as the 1-diisopropylphenyl-3-adamantyl substituted entity **I-28** (Scheme 6, bottom) a different strategy has to be utilized. One

possibility was developed by Fürstner *et al.* that is synthetically more complex, but also very flexible in terms of its product scope.[24-25] The method relies on the synthesis of an intermediate oxazolium moiety that its subsequently reacted to the imidazolium salt *via* an amine-induced heterocycle-interconversion.[24] The cascade is initiated by the reaction of an amine with commercial bromoacetaldehyde diethylacetal and followed by an *N*-formylation prior to treatment with acetic anhydride in the presence of a strong mineral acid. The resulting intermediate acetal is treated with a second amine of choice to yield the respective hydroxylated imidazolium scaffold that is finally dehydrated with acetic anhydride to afford the unsymmetrical precarbenic system **I-28** (Scheme 6, bottom). The benefit of this approach is its intrinsically modular character such that alkyl-substituents can conveniently be introduced into the backbone during the synthesis. For that, a slightly modified reaction protocol is followed, where an amine is reacted with an α-hydroxyketone to afford an α-aminoketone which is *N*-formylated to yield an analogous building unit that can be cyclized to the corresponding oxazolium salt.

In case 1,3-dialkyl-, or 1-alkyl-3-aryl-substituted ligand precursors are envisioned, the approach described above is not applicable in most cases. Thus, two different routes for this class of imidazolium salt were developed. The first one was reported by Gridnev *et al.* and consists of a very elegant one-pot setup for the synthesis of 1-alkylimidazoles **I-29** followed by their quaternization.[26] For the cyclization a mixture of the amine of choice, paraformaldehyde and ammonium chloride is reacted under acidic conditions (Scheme 7, top left). For 1-aryl-substituted congeners, an adapted procedure was developed allowing for their synthesis in good yields.[27]
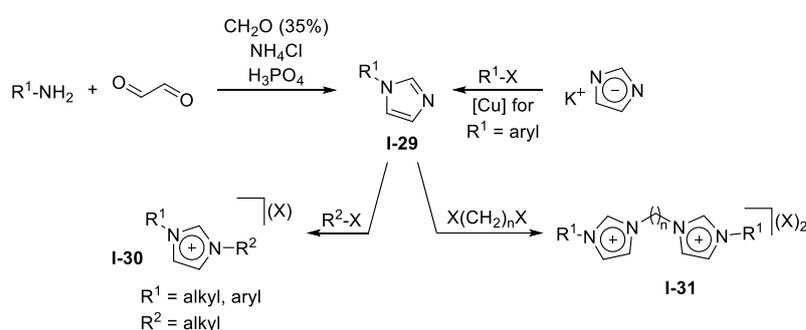
Scheme 7. General approaches for the synthesis of dialkyl- or alkyl/aryl-substituted imidazolium salts.[26-28]

Another possibility for accessing these alkyl-, or mixed aryl-alkyl-substituted precarbenes is the reaction of an alkali metal imidazolide with a suitable alkylating reagent (Scheme 7, top right). Accordingly, aryl electrophiles can be coupled to the imidazolide *via* a copper-catalyzed Ullmann-type reaction.[28c] A nucleophilic substitution between the 1-substituted imidazoles **I-29** and suitable electrophiles, commonly alkyl (pseudo)halides,[28a] in special cases even aryl halides,[28d] yields the desired ligand precursor salts **I-30** in a very straightforward and atom economical manner (Scheme 7, bottom left). Upon application of dihaloalkyl reagents, bridged bis(imidazolium) salts **I-31** are obtained (Scheme 7, bottom right).[28b]

The methylene bis(imidazole) entity **I-32** that is conveniently accessible in large scales, was shown to be a valuable starting material for a variety of powerful precursors for macrocyclic, or open-chain poly(NHC) complexes depending on its subsequent functionalization. When reacting it with alkyl bis(trifluoromethanesulfonates) of different chain lengths in preferably diluted solutions at low temperatures, alkyl-bridged tetraimidazolium salts **I-33** are obtained as reported

by the groups of Kühn and Jenkins (Scheme 8, top).[29] Likewise, these macrocycles can selectively be isolated *via* a template-strategy employing methylenbromide as electrophile and different tetrabutyl ammonium halides as templates.[30] The chemistry of these scaffolds will be discussed in greater detail in chapter 2.5. More recently, is was shown by Kühn *et al.* that a selective mono-methylation of **I-32** is possible upon reaction with iodomethane yielding the unsymmetrically substituted mono(imidazolium) iodide **I-34**.[31] As this molecule still contains one nucleophilic nitrogen site, it was further reacted with dibromomethane, or 1,3-dibromopropane, respectively, resulting in acyclic tetra(imidazolium) salts **I-35** (Scheme 8, bottom).
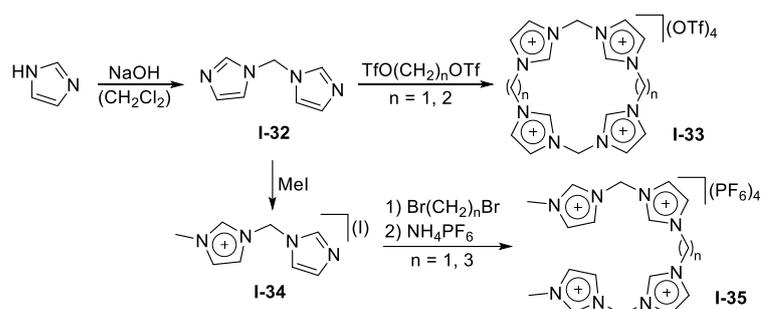
Scheme 8.　　Synthetic routes to macrocyclic and open-chain tetraimidazolium salts *via* the common precursor methylene bis(imidazole) **I-32**.[29,31]

Apart from the simple imidazolium salts with hydrogen atoms bound to the backbone carbon atoms, benzimidazolium scaffolds and their derivatives are frequently encountered systems, as they allow for a manifold of further ligand modifications in terms of structural extensions or elements influencing the ligand's steric or electronic properties.[32] Bielawski *et al.* were able to synthesize the quinone-annulated imidazolium **I-36** scaffold by a condensation reaction of *N,N*-dimesityl-formamidine and 2,3-dichloro-1,4-naphthoquinone (Scheme 9, top).[33] The best yields were obtained when adding one additional equivalent formamidine as sacrificial base that can be recovered with NaHCO₃ after the reaction.[34] This procedure was further developed and expanded to a wider scope of diarylformamidines by Glorius *et al.* which enabled the isolation of a range of unsymmetrical aryl substituted imidazolium salts with various backbone substitution patterns.[35]
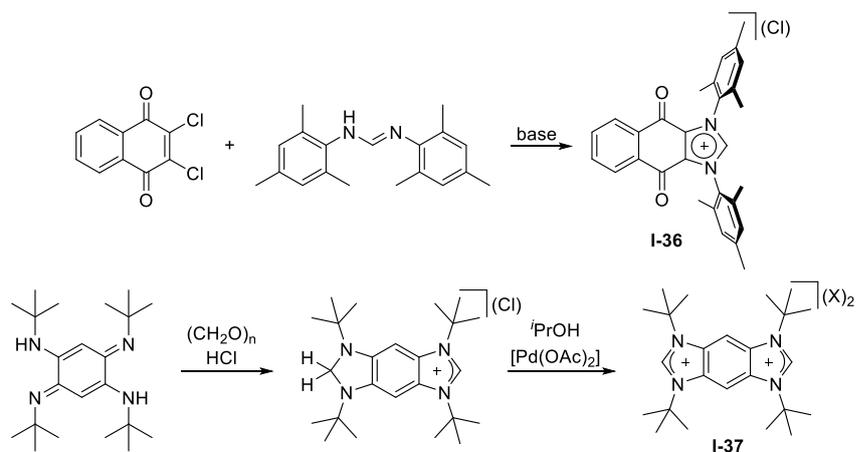
Scheme 9.　　Top: Backbone introduction to dimesitylformamidine as percarbenic diamino entity to yield the quinone-annulated imidazolium scaffold **I-36**.[33-34] Bottom: One-pot cyclization/oxidation reaction cascade to afford benzobis(imidazolium) salt **I-37**.[36]

The paraformaldehyde route described above is likewise applicable for the synthesis of benzimidazolium derivatives. The condensation of *N,N'*-disubstituted 1,2-diaminobenzenes with aqueous formaldehyde generally yields the corresponding benzimidazolines which can be treated with an oxidant, such as trityl tetrafluoroborate, to obtain the respective benzimidazolium tetrafluoroborates.[37] An analogous cyclization reaction was carried out on 2,5-diamino-1,4-benzoquinonediimines (*via* an intrinsic *ortho*- and *para*-quinoid equilibrium) to yield annulated benzimidazolium/*N,N'*-aminal hybrids.[36b] The following Pd-catalyzed oxidation of these intermediates afforded the respective benzobis(imidazolium) salts, such as **I-37** (Scheme 9, bottom).[36a]

The related class of imidazolinium salts featuring a saturated backbone, are generally accessible *via* a modified glyoxal route first reported by Arduengo and co-workers (Scheme 10, top).[23] For that, the respective diimine is synthesized in an analogous way by reacting a suitable amine with glyoxal.[38] Subsequently, it is treated with a reducing agent, such as sodium borohydride, to obtain the corresponding diamine (usually isolated as hydrochloride salt). The cyclization is induced by the addition of the C1 building block triethyl orthoformate that readily affords the imidazolinium scaffold **I-38** in overall high yields.[23,39] For unsymmetrical congeners of this class one common strategy is the utilization of a Boc-protected amine which is reacted with a 1-amino-2-haloethane (Scheme 10, bottom).[40] Subsequent acidic deprotection and cyclization with HC(OEt)$_3$ produces the desired azolinium salts **I-39**.
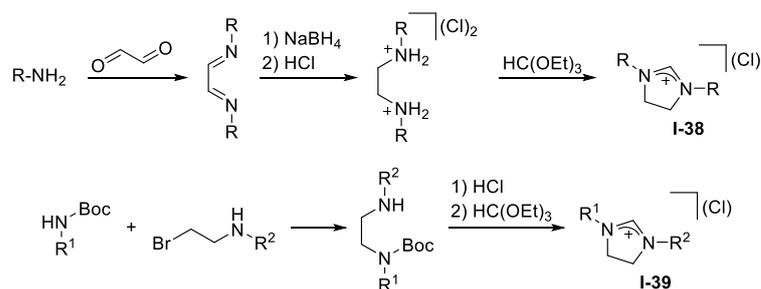
Scheme 10. General approaches for the synthesis of symmetrical and unsymmetrical imidazolinium salts.[23,40]

2.2.2 Synthetic Routes to NHC Complexes

With an ever growing number of NHC ligand modifications in terms of their electronic and steric properties, eventually novel synthetic strategies for the respective metal complexes had to be developed, as established ones might be low yielding or even inoperative for specific ligand classes or certain metal precursors. However, several approaches have proven themselves widely applicable for the synthesis of NHC complexes and shall be described in the following chapter.

2.2.2.1 Free carbenes

Free carbenes are generally accessible by C–H deprotonation of the corresponding imidazolium salts with strong bases, such as KO'Bu, LDA, Na/KBTSA, or NaH.[4b,41] They can often be readily isolated and stored indefinitely under inert conditions without decomposition. For the synthesis of metal complexes the utilization of free carbenes as starting materials over imidazolium salts has certain advantages, for example their better solubility in organic solvents and cleaner complex formation due to the avoidance of anion scrambling and the addition of bases.[42] Arduengo *et al.* were the first to isolate a free *N*-heterocyclic carbene in 1991, namely the 1,3-diadamantylimidazolylidene **I-48**, by deprotonation of the respective imidazolium chloride **I-47** with sodium hydride in the presence of catalytic amounts of dimethyl sulfoxide.[4b] Subsequently, the free carbene could be utilized for metal-coordination to access novel organometallic compounds, such as the zinc NHC complex **I-49** (Scheme 11, bottom).[43] Oftentimes, a weaker coordinating ligand is displaced upon reaction of a free NHC with a suitable, coordinatively saturated metal precursor. Exemplarily, Herrmann *et al.* reacted the simple 1,3-dimethyl-imidazolylidene with a variety of metal carbonyl complexes and observed the formation of NHC complexes, such as **I-41** and **I-43** under liberation of one CO ligand in each case (Scheme 11, left).[5a] As was also shown in this report, it is possible to displace more than one carbonyl moiety when employing overstochiometric amounts of free carbene to form di(carbenes), such as **I-42**. Later on, similar results were found by Nolan and co-workers.[44] Additionally, they showed that upon reacting a free carbene with very bulky wingtips, for example adamantly or *tert*-butyl, with nickel(0) tetracarbonyl, the ligand displaces two CO ligands simultaneously and affords a three-coordinate nickel(0) complex.[45] The free NHC **I-40** could also be used for the synthesis of mono(carbene) complexes of Ru and Os, as well as di(carbene) complexes of Rh.[42]
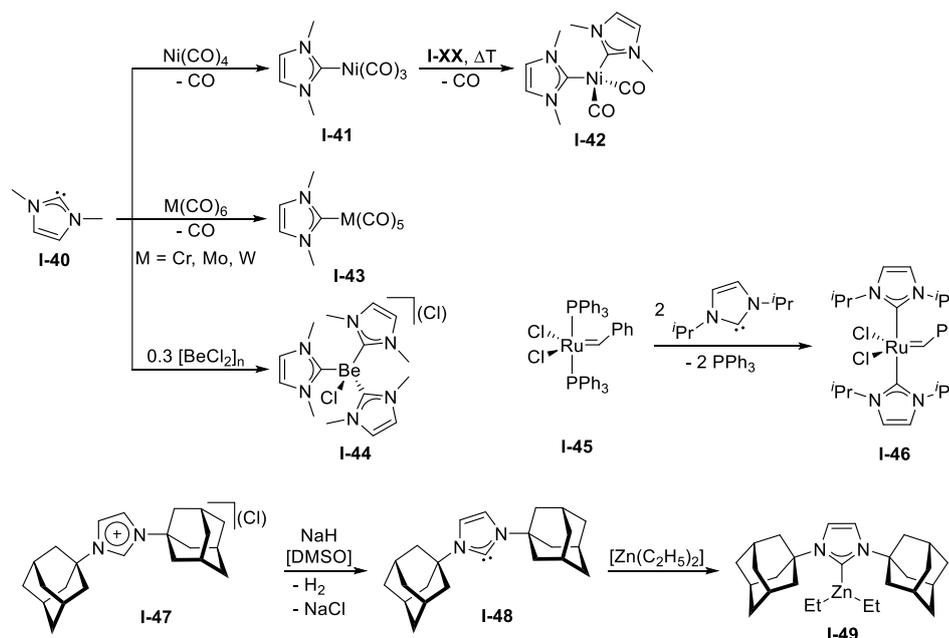

Scheme 11.   Selected examples for the synthesis of metal complexes employing free NHCs.[4b,5a,43,45-46]

N-heterocyclic carbenes have been employed for a multitude of ligand substitution reactions where weaker binding ligand other than CO are displaced, such as phosphines, for example during

the synthesis of ruthenium NHC complex **I-46** from **I-45** and 1,3-diisopropylimidazolylidene (Scheme 11, right).[46] A highly important contribution was achieved by Herrmann *et al.* with the successful isolation of the Be^{II} complex **I-44** *via* reaction of beryllium chloride and the free carbene **I-40** (Scheme 11, left).[47] This finding made it clear for the first time that the *N*-heterocyclic carbenes derived from imidazole scaffolds do not depend on backbonding upon forming stable complexes and thus cannot be compared with Schrock-,[48] or Fischer-type carbenes,[49] but are similar to phosphines in terms of their coordination chemistry and metal-binding properties.[9a] The approach to use free carbenes as starting materials for metal coordination can also be extended to multidentate ligands, such as 2,6-bis[(diisopropylphenyl)imidazolylidene]pyridine, as was demonstrated by Danopoulos *et al.* for Fe and Ru complexes,[50] and by Gibson *et al.* for a series of Ti, V, Cr, Co, and Fe compounds.[51]

2.2.2.2 Internal bases

A common approach for the synthesis of *N*-heterocyclic carbene complexes is the utilization of metal precursors containing basic ligands, such as alkoxo, acetato, hydrido, hydroxido, or oxo moieties. In fact, the very first NHC metal complexes, namely the chromium compound **I-51** by Öfele[2a] and the mercury complex **I-53** by Wanzlick *et al.*,[2b] were synthesized *via* this method in 1968 (Scheme 12). The utilized imidazolium metal hydride salt **I-50** releases molecular hydrogen upon heating while forming the respective imidazolylidene complex **I-51**, instead of resulting in a dihydroheterocyclic entity π-bound to a chromium tricarbonyl fragment, as was observed for analogous *N*-methyl pyridinium cations.[2a] In the Wanzlick-case, the acetate anions of the mercury precursor salt are sufficiently basic to deprotonate the diphenylimdiazolium cation **I-52**, wherefrom the di(carbene) complex **I-53** and two equivalents of acetic acid are formed.[2b]
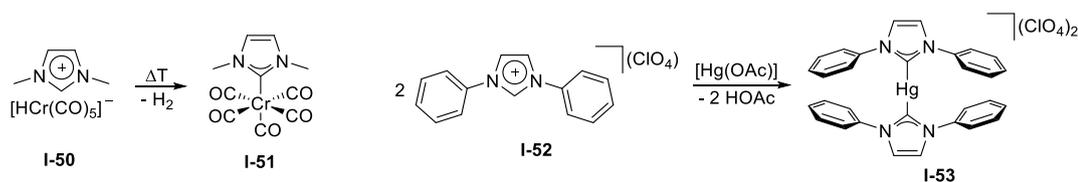
Scheme 12.   First reported syntheses of NHC complexes **I-51** by Öfele and **I-53** by Wanzlick *et al.*, both obtained *via* deprotonation of the ligand precursors by internal bases.[2]

Decades later, this principle is now widely applied for the synthesis of NHC complexes. Before all, acetates were shown to be suitable for this purpose. Exemplarily, the first Pd NHC complexes used as catalysts for Heck-type reactions were synthesized from Pd(OAc)$_2$, such as di(carbene) compound **I-54** (Scheme 13, top left).[52] Metal precursors featuring basic hydrido ligands represent an even more elegant deprotonation technique as the only byproduct is gaseous H$_2$. It is often applied for the synthesis of iridium NHC complexes due to the ready availability of Ir hydride precursors, such as [IrH$_5$(PPh$_3$)$_2$] used by Crabtree *et al.* for the synthesis of pyridyl-substituted imidazolylidene complexes.[53] In this particular case, formation of both the normal carbene **I-55**, as well as the abnormal congener **I-55a** was observed (Scheme 13, top right). Furthermore, alkoxo ligands of short chain length, are highly suitable basic ligands, as the corresponding acids are simple alcohols, which are generally well separable from the product. One example is the rhodium imidazolylidene complex **I-56** reported by Herrmann *et al.*, that was obtained *via* reacting the

respective imidazolium halides with [Rh(OEt)$_2$(COD)]$_2$ (Scheme 13, bottom left).[54] However, the arguably most applied metal precursor for this purpose is silver(I) oxide. The basicity of the oxo anions is generally sufficient for a twofold deprotonation, ultimately yielding water as the only by-product. The resulting silver NHC complexes, such as compound **I-57**,[55] are very prominent synthetic targets, as they can be employed in ligand transfer reactions (see chapter 2.2.2.3).
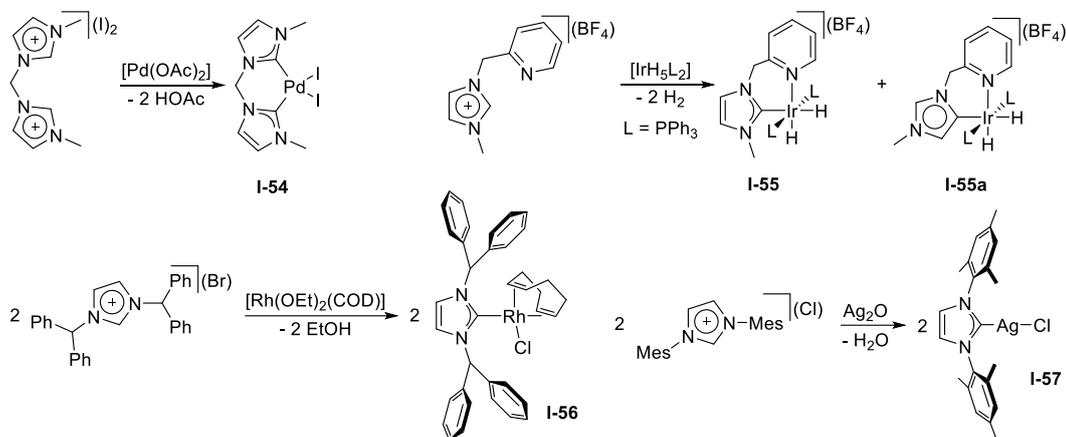

Scheme 13. Further examples of NHC complexes synthesized with metal precursors featuring internal bases.[52a,53-55]

2.2.2.3 Transmetalation

The isolation of silver(I) complexes is a central cornerstone of NHC chemistry, because it allows for ligand transfer reactions to a plethora of other transition metals under precipitation of silver halides as driving force.[8b,56] This is additionally beneficial, since these complexes are conveniently accessible by reaction of imidazolium salts with silver(I) oxide, as described in the previous section. Moreover, these species are usually thermodynamically very stable allowing for reaction setups under non-inert conditions. The respective silver NHC complex to be transmetalated can either be isolated, or prepared *in situ* and further reacted immediately. The first successful Ag-transfer reaction was reported by Lin *et al.* in 1998,[57] where they synthesized a [Ag(NHC)$_2$][AgX$_2$]-type complex **I-58** bearing benzimidazolylidene ligands that could readily be transferred to palladium(II) and gold(I) with the precursors [PdCl$_2$(MeCN)$_2$] and [AuCl(SMe$_2$)] resulting in the transmetalation products **I-59** and **I-60**, respectively (Scheme 14, top). This method is applicable not only to mononuclear silver NHCs, but also to systems with multiple silver centers, such as binuclear complex **I-61**, that is converted to the Rh compound **I-62** upon ligand transfer, as shown by Slaughter and co-workers (Scheme 14, middle).[58] Later on, it was demonstrated by Crabtree *et al.* that the length of the alkyl chain between the imidazole heterocycles, as well as the *N*-wingtips have crucial influence on the structural outcome of the transmetalation by isolating also dinuclear Rh NHC complexes in certain cases.[59] Especially for functionalized NHCs, the structural composition of the transmetalation product is oftentimes heavily depending on the nature of the metal precursor, the reaction conditions, as well as the stoichiometries of the reactants applied in the carbene transfer reaction. For example, Cavell *et al.* showed that equimolar reactions of the picolyl substituted silver complex **I-63** with [PdCl$_2$(MeCN)$_2$] or [PdClMe(COD)] produced non-chelated, di(carbene) complexes **I-64** and **I-65**, respectively, the former with the two NHC

ligands in *cis*-position (Scheme 14, bottom left), the latter with the carbenes *trans* to each other (Scheme 14, bottom middle).[60] The chelated mono(carbene) complex **I-66**, however, was obtained upon reaction of **I-63** with two equivalents of [PdClMe(COD)] (Scheme 14, bottom right). In principle, a carbene exchange from complexes with other metal centers apart from silver(I) has been demonstrated, however, these approaches lack the broad applicability of the Ag-transfer route.[61]
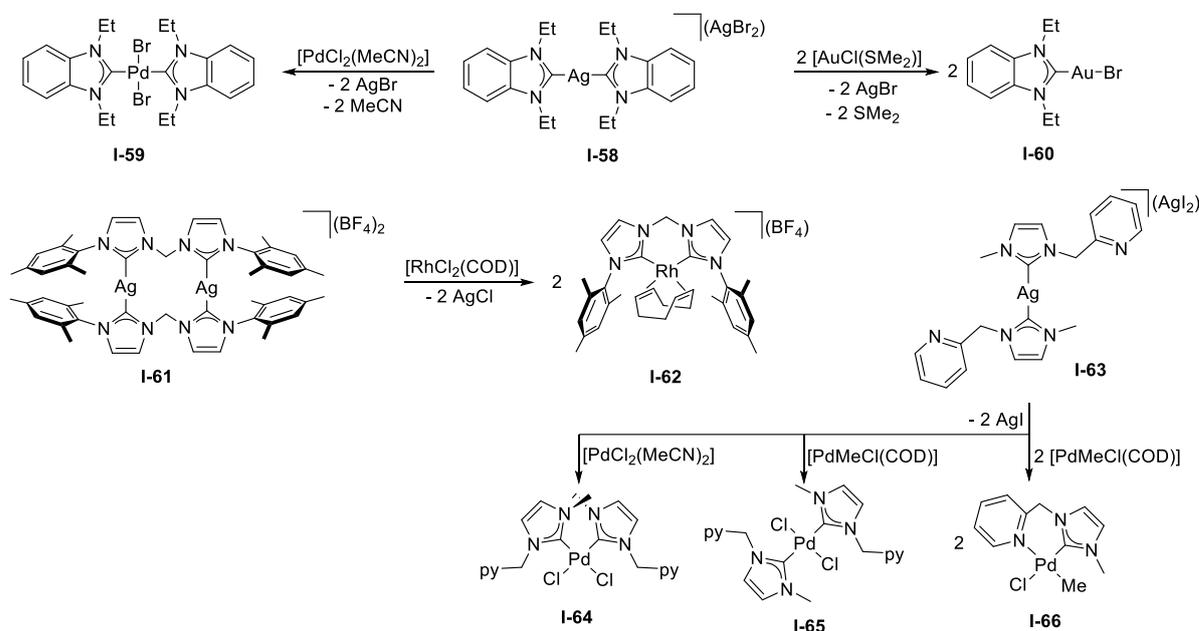
Scheme 14. Transmetalation reactions from silver(I) complexes as carbene sources.[57-58,60]

2.2.2.4 External bases

The huge benefit of the NHC metal complex synthesis through addition of external bases is certainly the great variability in terms of choosing a suitable reagent for specific needs, since numerous bases over a broad pK_a range are (commercially) available. This approach is arguably amongst the most widely applied strategies, presumably also due to the fact that it was discovered and established relatively early by Herrmann and co-workers,[5a] who employed very strong bases, such as NaH, KO^{t}Bu, or mixtures thereof for the synthesis of NHC complexes.
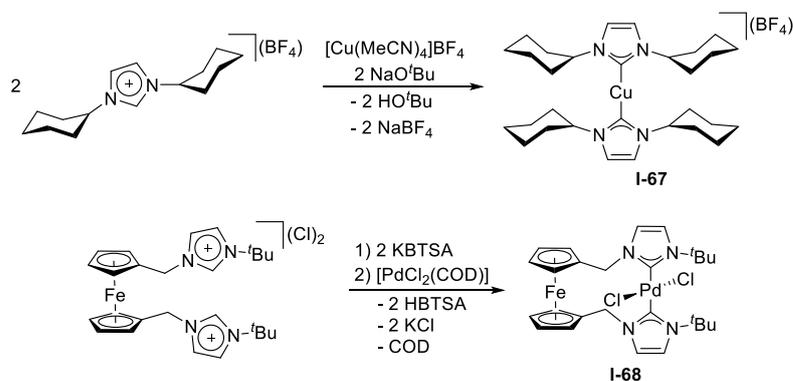
Scheme 15. Synthesis of NHC complexes by *in situ* carbene formation employing strong external bases.[62]

In order to avoid side-reactions strong bases applicable for this purpose are generally sterically demanding, for example KBTSA, LDA, or KO*t*Bu. Nolan *et al.* synthesized various [Cu^I(NHC)$_2$]-type compounds, such as **I-67** (Scheme 15, top), as catalysts for hydrosilylation reactions.[62b] The best results were obtained for reaction mixtures containing the respective imidazolium tetrafluoroborate, [Cu(MeCN)$_4$]BF$_4$ and NaO*t*Bu as base. Another example was reported by Coleman and co-workers, namely the synthesis of the ferrocenyl-bridged di(NHC) complex **I-68** *via* reaction of the respective imidazolium salt with [PdCl$_2$(COD)] in the presence of KBTSA.[62a] One major disadvantage of employing strong bases in these reaction mixtures is the fact that the starting materials' stoichiometry needs to be matched meticulously, as in the case of excess base side-reactions occur readily in many cases. Additionally, low temperatures and absolute solvents are usually a prerequisite for reactions involving strong bases.

However, it was shown that an excess of weak bases likewise allows for the synthesis of NHC complexes, commonly at higher temperatures. The pK_a values of these bases are lower by several orders of magnitude compared to the pK_a of the imidazolium cations and therefore their deprotonation should not occur. Nonetheless, the use of excessive base and elevated temperatures, as well as the formation of a thermodynamically favored metal carbene bond leads to the continuous removal of nascent free NHCs from the equilibrium and thus the reaction is driven to the product side. By this approach, the ruthenium(II) complex **I-69** reported by Peris *et al.* was obtained as the exclusive product upon reaction of the respective ethylene-bridged bis(imidazolium) salt with [RuCl$_2$(η^6-*p*-cymene)]$_2$ in the presence of excess triethyl amine (Scheme 16, left).[63] It was suggested that the deprotonation of the precursor is favored by its fast coordination to the metal, thus displacing the equilibrium to the di(carbene) formation without the formation of intermediary free NHCs. Analogously, the same group synthesized the Ir^{III} complex **I-70** employing sodium acetate as weak base (Scheme 16, right).[64] Next to the deprotonation of the imidazolium cation a C–H activation at one of the phenyl substituents was observed in this example. A possible drawback of this route is the fact that the purification of the products is more challenging in certain cases.
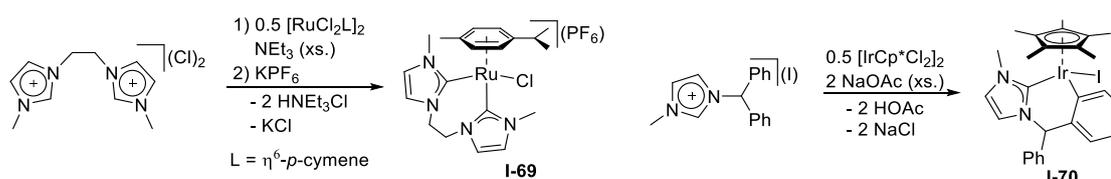
Scheme 16.   Synthesis of NHC complexes by *in situ* carbene formation employing weak external bases.[63-64]

2.2.2.5 *Oxidative addition*

The first reports of oxidative additions of 2-chloro derivatives of different *N*-heterocycles to Ir, Pd, Pt, and Ni complexes surfaced already more than 40 years ago,[65] however, they have not received considerable attention as general access route to NHC complexes of late transition metals. Only after Yates *et al.* demonstrated in 2001 experimentally and theoretically that the oxidative addition of C2–H and C2–I bonds of imidazolium cations to electron rich d^{10} metals is not only possible, but also energetically favored in certain cases,[66] this method became a viable access route

for NHC metal complexes. Subsequently, it was shown that the utilization of coordinatively unsaturated metal precursors, such as [Pt(PPh$_3$)$_2$] instead of [Pt(PPh$_3$)$_4$] facilitates the oxidative addition.[66a]
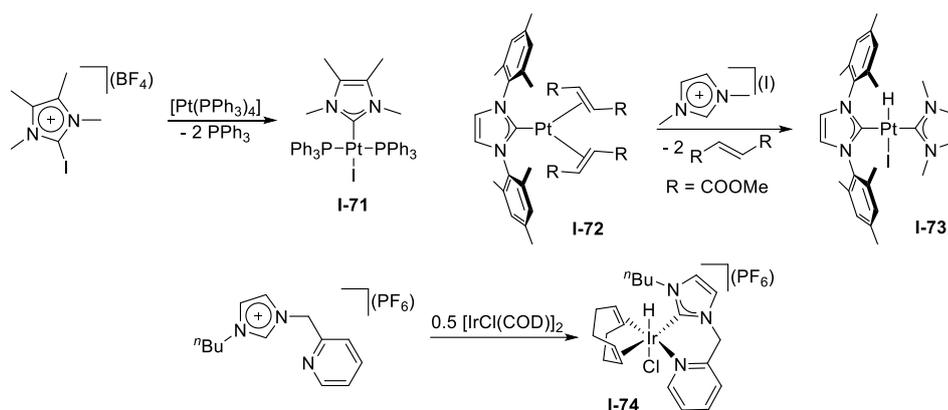
Scheme 17.   Synthesis of NHC complexes *via* oxidative addition to electron rich metal centers.[66a,67]

As suggested by DFT calculations, the oxidative addition of C2–X (X = halogen) bonds to Pt^0 centers proceeds smoothly to yield the respective Pt^{II} NHC complex, as shown by Yates *et al.* by isolation of complex **I-71** through reaction of [Pt(PPh$_3$)$_4$] with an 2-iodoimidazolium salt (Scheme 17, top left).[66a] Likewise, the palladium(II) congener was prepared *via* this route.[66b,66c] Cavell, Elsevier and co-workers used Pt^0 di(NHC) complexes, such as **I-72**, as starting materials for the oxidative addition of a third imidazolium entity.[67a] Thereby, they demonstrated that these zerovalent mono(carbene) complexes readily activate the C2–H bonds of imidazolium salts already at room temperature under formation of thermally stable platinum(II) hydrido compounds like **I-73** with the two NHC ligands bound in *trans* position to each other (Scheme 17, top right). Functionalized imidazolium salts with additional neutral donor sites, for example pyridine entities, are more reactive towards an oxidative addition. Exemplarily, Peris *et al.* employed *N*-picolyl substituted precursors for the reaction with [IrCl(COD)]$_2$ to obtain Ir^{III} chelate complexes, such as **I-74**, in good yields (Scheme 17, bottom).[67b] It was reasoned that the *N*-donor of the pyridyl moiety coordinates to the metal center bringing the C2–H bond in close proximity to the metal center and thus facilitates its oxidative addition. With rhodium(I) no reaction occurred under analogous conditions.

2.2.2.6 Other strategies

Besides the most frequently encountered approaches for the synthesis of NHC complexes described above, further less common methods have been developed over the last decades.[68] One route is the synthesis of so-called protected carbenes which are adducts that form upon reaction of a free carbene with suitable reagents, such as alcohols,[69] perfluoroarenes,[70] trialkylboranes,[61c] hydrogen cyanide,[71] or ammonia.[13c] Their shared principle is the formation of the free carbene *via* liberation of the protecting entity at elevated temperatures that allows for a subsequent reaction with a suitable metal precursor. Another technique that was introduced by Lappert *et al.* and was widely used before the isolation of free *N*-heterocyclic carbenes initiated more advanced methods, is the insertion of metal ions into electron rich olefins within tertaamine scaffolds, so-called

enetetramines.[3a,72] It is still applied at times, for example for the synthesis of water-soluble ruthenium NHC complexes.[73] A very elegant, yet limited approach by Fehlhammer *et al.* relies on the stepwise synthesis of the NHC ligand directly at the metal center *via* cyclization of coordinated isocyanides.[74] This on-site synthetic cascade will be discussed in greater detail in chapter 2.5.2.

2.3   Electronic Properties

One decisive property of *N*-heterocyclic carbenes is their exceptional electron richness.[9a] This property is certainly one of the reasons NHCs gained the importance they have today. The understanding of its origin and their exploitation are crucial factors for the design of functional metal complexes. Thus, the following section provides an in-depth description of the electronic features contributing to the stabilization of the carbene center, the factors influencing the ligands' donor strength and the measurement techniques thereof, as well as synthetic strategies to adjust and fine-tune the electronic situation within the heterocyclic scaffold.

2.3.1 Stabilization

The carbene carbon donor atom in *N*-heterocyclic carbenes is nucleophilic rather than electrophilic, thus they are not considered Fischer-type carbenes,[49,75] albeit the have singlet character and certain similarities between NHC-related diaminocarbenes and Fischer carbenes were observed.[76] In turn, they cannot be classified as Schrock carbenes, as this group's common property is the triplet ground state of the carbene.[48] Therefore, *N*-heterocyclic carbenes form their own class of nucleophilic singlet carbenes.

Initially, it was commonly believed that bulky *N*-substituents that prevent dimerization (the Wanzlick equilibrium)[77] through sterical protection, are a crucial factor for the isolation of free stable carbenes.[4b] However, this assumption had to be revised when the first free NHCs with only methyl groups as wingtips were successfully isolated.[5a,78] Additionally, free stable examples of saturated *N*-heterocyclic carbenes indicated that an aromaticity in the heterocyclic system is not a prerequisite for their feasibility.[79] These results were the basis for extensive theoretical investigations with the aim to explain the underlying properties of these compounds that grants their immense stability. The first important finding was that a singlet state is the preferred electronical configuration for the electron sextet located at the carbene carbon. The N–C–N angles found in the crystal structures of the first free NHCs confirm this presumption.[80] As a triplet configuration is necessary for an irreversible dimerization of two free carbenes, the energy gap between the singlet and triplet state was defined accordingly as one theoretical indicator for carbene stability.[80-81] The singlet-triplet gaps of frequently encountered NHCs are typically in the range of 65 kcal mol^{-1} rendering the unfavorable triplet state inaccessible at room temperature.[82]

To further elucidate the causes of the electronic stabilization observed in the carbenes considerable theoretical as well as experimental efforts have been made to examine the various electronic contributions of all parts of the heterocycle.[82-83] The predominant electronic interaction

responsible for the observed properties was found to be located within the N–C–N unit of the imidazole ring. On the one hand, a σ-electron withdrawal from the carbene center is caused by the adjacent nitrogen atoms being more electronegative than carbon. But on the other hand and more importantly, the formally empty p-orbital of the carbene carbon atom receives a strong back-donation of electron density from the nitrogen's lone pairs *via* the π-system. Consequently, the ensemble of these effects lead to a singlet ground-state with the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO) best described as a formally sp^2-hybridized lone pair and an unoccupied p-orbital at the C2 carbon atom, respectively. The resulting electron delocalization over the N–C–N moiety is the main criterion for stability (Figure 11, 1).[83]
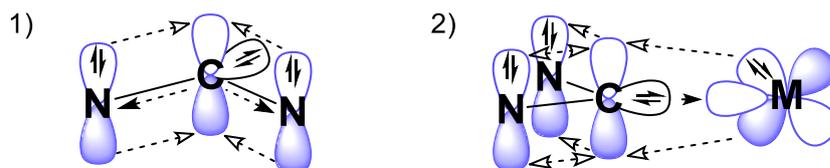

Figure 11. Important electronic interactions responsible for the stability of *N*-heterocyclic carbenes: 1) Electron donation from the nitrogen lone pairs to the empty orbital of the carbene carbon within the N–C–N unit.[84] 2) σ-bonding from the singlet carbene lone pair to the metal orbital and π-backbonding from metal d-orbital to the empty orbital of the carbene carbon atom. Full arrowheads indicate σ-interaction, hollow arrowheads π-interaction.

Further studies revealed that a stabilization by aromaticity in scaffolds featuring an olefinic backbone leads to an energy gain of approximately 25 kcal mol^{-1} compared to the saturated congeners with an enhanced σ-character.[82,85] The amount of aromatic electron delocalization throughout the heterocyclic scaffold was determined with the aid of the molecule's magnetic susceptibilities.[83] The anisotropies were calculated to approximately 60 % of the benzene value suggesting a substantial aromatic character.

The main electronic contribution to the carbene metal bond is caused by a σ-type donation of the carbene's free electron pair to suitable metal orbitals with σ-character (Figure 11, 2) The successful isolation of beryllium NHC complexes elegantly demonstrated that this σ-electron donation is sufficient to maintain a carbon metal bond without the aid of π-backbonding admixtures from the metal center.[47] It was, however, observed several times that a π-backbonding may contribute up to a third of the overall bonding interactions, especially for electron rich metal centers (Figure 11, 2).[33,86]

I-75
ν(C=O) = 1670 cm^{-1}

I-76
ν(C=O) = 1680 cm^{-1}
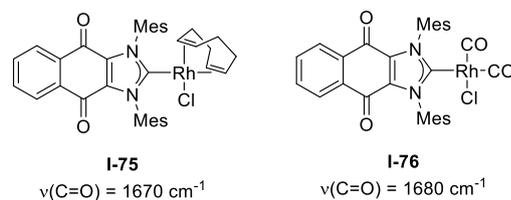
Figure 12. Rhodium NHC complexes **I-75** and **I-76** that allow for the quantification of metal to carbene π-backbonding effects *via* IR spectroscopic measurements.[33]

Exemplarily, one experimental method to straightforwardly measure the extent of metal to carbene π-backbonding was reported by Bielawski *et al.* and relies on the rhodium complexes **I-75** and **I-76** featuring a quinone-based NHC ligand (Figure 12).[33] The simple ligand exchange from

COD to two carbonyl entities causes a significant reduction of the electron density at the Rh center. Consequently, this entails a reduction of the π-back-donation to the *N*-heterocyclic ligand which was monitored by a shift of the quinone's carbonyl resonance in the IR spectrum.

2.3.2 σ-donor strength

The donor strength of *N*-heterocyclic carbenes depends heavily on the nature of the heterocycles and their substituents. In order to assess the ligands' donor capabilities different approaches have been developed during the last two decades.[87] One relatively new method relies on the measurement of the carbene carbon atoms' chemical shift (Figure 13, left, highlighted in blue) in a benzimidazolylidene palladium(II) complex *via* ^{13}C NMR spectroscopy. The NHC ligand of interest is bound in *trans*-position to this sensor ligand affecting its carbon resonance through the *trans*-effect across the metal center.[88] Utilizing this method first reported in 2009, Huynh *et al.* examined the electronic properties of several NHC ligands in these heterodi(carbene) palladium(II) complexes.[89]
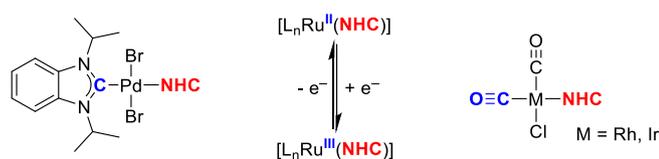

Figure 13.   Methods for the determination of the donor strength of NHCs.

Another useful technique developed by Lever *et al.* is based on the determination of the E_0 values for Ru[II]/Ru[III] redox pairs of various compounds that contain the ligand of interest (Figure 13, middle).[90] After conversion of the obtained data into the Lever electronic parameter (LEP) it is theoretically possible to compare those values to that of other ligand classes, however, only few ligands have been analyzed to date.[91] Certainly, the most applied technique for the measurement of electron donating capability of such monodentate ligands is the synthesis and vibration-spectroscopic analysis of carbonyl complexes featuring these ligand entities. Initially, [Ni(CO)$_3$L]-type compounds were employed for this purpose. The method relies on the property of carbonyl compounds that electron density is transferred not only onto the metal center, but also into the π* orbital of a CO ligand, caused by backbonding effects from the metal ion to the carbonyl group. As the stretching vibration of carbon monoxide (ν_{CO}) gives rise to very prominent signals in the respective IR spectrum, this resonance can be used as an analytic handle to assess ligands' donor strength. With an increasing donation of electron density from the ligand the wavenumber of ν_{CO} is reduced due to a weakening of the CO bond. This easily measurable feature is referred to as Tolman electronic parameter (TEP) and is proportional to the donor strength (Figure 13, right).[92] In the case of NHC ligands the handling of the corresponding Ni[0] complexes was found to be problematic due to their toxicity and stability issues. Thus, they were subsequently replaced by [Ir[I]Cl(CO)$_2$(NHC)]- and [Rh[I]Cl(CO)$_2$(NHC)]-type compounds which are easier to handle in terms of safety and stability. The vibrational data obtained by this modified technique can conveniently be converted into TEP values based on studies by Crabtree *et al.* and Nolan *et al.*[93] Later, Cenio *et al.* presented additional equations that allowed for a correlation between iridium- and rhodium-

based systems.[94] Based on this plethora of experimental data the TEP values were shown to be readily accessible by theoretical calculations.[95] These results generally show an excellent comparability as well as high time efficiency and thus became a powerful screening method for the selection of synthetic targets featuring the desired properties.
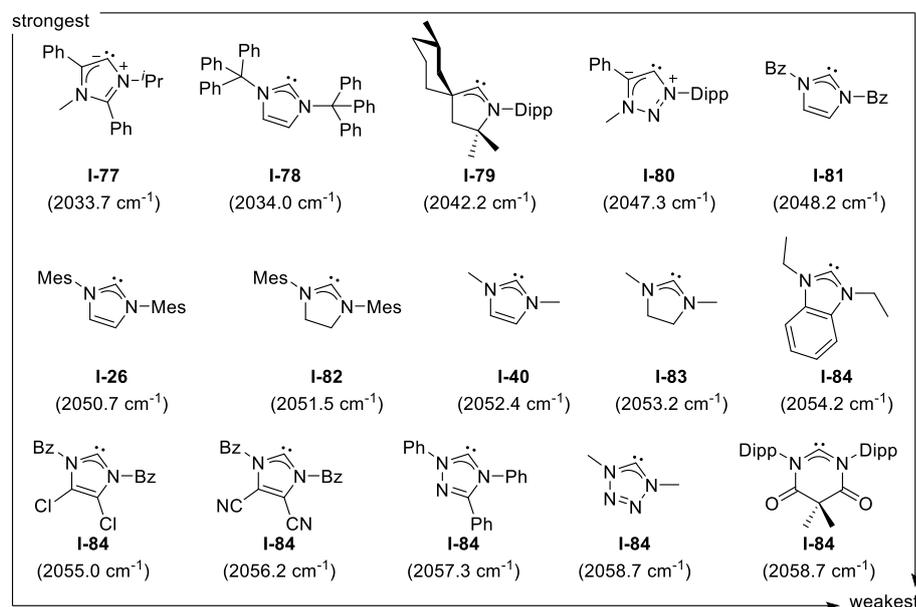

Figure 14.   Selection of NHCs and their respective donor strength given in TEP values descending with the strongest donor on the top left and the weakest on the bottom right.[13a,15b,96]

The TEP values obtained for NHCs ligands unequivocally proof their electron richness. The majority of carbenes derived from *N*-heterocycles show a significantly higher donor strength than phosphine ligands. Exemplarily, the TEP of the omnipresent triphenyl phosphine PPh$_3$ amounts to 2068.9 cm^{-1}.[92] The data furthermore indicates that the wingtip substituents at the heteroatoms have generally only minor influence on the ligand's electronic properties, such that the donor strength of **I-26**, **I-40**, and **I-81** are very similar (Figure 14). This is likely due to the fact that these substituents are not directly bound to the donor atom, but rather in the periphery of the ligand system. This observation is highly beneficial, because it allows for an orthogonal tuning of the sterical demand *via* wingtip modifications without altering the donor features of the carbene. However, other factors influence the electronic situation in the heterocycle more or less strongly, a selection of which will be discussed in the following paragraph.

2.3.3 Electronic Tunability

As mentioned above, the wingtip substituent has little impact on the overall electronic situation of the ligand in most cases. This feature can be exploited for a meticulous fine-tuning of the donor strength in order to obtain the ideal ligand properties for the desired application. In a systematic study Plenio *et al.* synthesized a variety of *N,N*-diarylated imidazolylidenes that differed solely in their *para*-substituent at the phenyl rings.[91] The determined TEP values suggest that the donor strength is increasing in the row SO$_2$Tol < Br < Me < H < OC$_{12}$H$_{25}$ < NEt$_2$, as is certainly expected upon comparison of the substituents' mesomeric and inductive effects on the aryl

wingtips. The difference between the two extreme entries was reported to be Δ(TEP) =7.2 cm^{-1}. Bertrand *et al.* observed similar effects upon variation of the boron substituents on boron-containing cyclic six-membered *N*-heterocycles (Δ(TEP)$_{max}$ =7.4 cm^{-1}).[97] A slightly different approach by Fürstner *et al.* relied on the tuning of though-space interactions in pyridine-derived imidazolylidenes.[98]

Another structural parameter influencing the donor properties of the heterocyclic scaffold that can readily be modified is the ligand's backbone. In contrast to wingtip variations, this adjustment generally leaves the sterical situation at the metal center unaltered due to the spacial distance, whereas the electronics of the ligand are affected to a certain extend. In accordance, studies by Glorius *et al.* revealed that an installing alkyl substituents of different length at the ligand's backbone has next to no effect on its donor strength.[99] Similar results were obtained by Organ *et al.* upon modification of the outermost aryl positions of benzimidazolylidene-based ligands.[100] Due to its large distance to the metal center the measured effect was not significant. However, a substantial effect was observed when placing substituents of strongly differing inductive and mesomeric effects onto the backbone of imidazolylidenes as shown by Herrmann *et al.* and Bielawski *et al.*[96,101]

Arguably one of the most decisive parameters influencing the donor strength of NHCs are the number and type of heteroatoms in the ligand framework, as well as their position(s) relative to the carbon donor atom(s). At the same time, this type of variation is certainly one of the most extensive featuring a plethora of possibilities and will only be discussed very briefly in this comprehensive introduction.[17a] Upon introducing chalcogens, such as oxygen and sulphur, into the scaffold, or exchanging backbone carbon atoms in the imidazolylidene moiety by more electronegative heteroatoms, usually very electron poor ligands are obtained as theoretical investigations indicated (Figure 15).[95c]


I-85
(2061.5 cm^{-1})

I-86
(2060.0 cm^{-1})

I-83
(2053.2 cm^{-1})

I-87
(2048.3 cm^{-1})

I-88
(2046.6 cm^{-1})

I-89
(2044.3 cm^{-1})

weaker ⟶ stronger

I-40
(2052.2 cm^{-1})

I-90
(2051.6 cm^{-1})

I-91
(2048.6 cm^{-1})

I-92
(2045.8 cm^{-1})

I-93
(2033.7 cm^{-1})
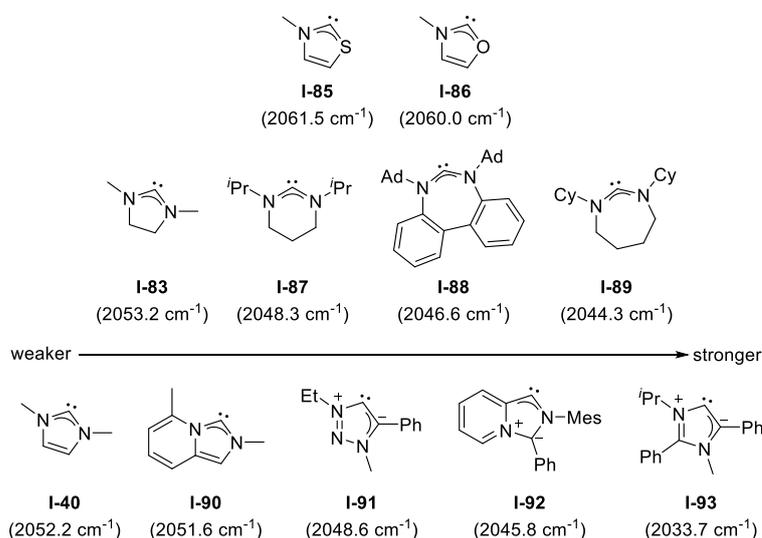
Figure 15. Top: Electron-poor, chalcogene-based NHC ligands **I-85** and **I-86** and their quantum chemically determined TEP values. Middle: Comparison of the donor strength of selected five-, six- and seven-membered NHC ligands **I-83**-**I-89**. Bottom: Comparison of the donor strength of some normal and abnormal NHC ligands **I-40**-**I-93**.[9d]

An expansion of the azole's ring size towards six- and seven-membered heterocycles leads to an increase of the donor strength.[95c,102] Furthermore, the abnormally pyridoanellated entity **I-92** reported by Lassaletta *et al.* is a much stronger donor than the normal congener **I-90** (Δ(TEP)$_{max}$ =

5.8 cm^{-1}). Amongst the abnormal NHCs the 1,2,3-triazolylidene **I-91** by Albrecht *et al.* is rather electron poor,[103] whereas the imidazolylidene **I-93** reported by Crabtree *et al.* is strongly donating.[104]

A further possibility to adjust the donor strength of NHCs in a very elegant way is the utilization of reversibly switchable substituents that effect the electronic properties of the scaffold. Bielawski *et al.* reported the ferrocene-based systems **I-94** and **I-95** that exhibit varying donor capabilities depending on the oxidation state of the ferrocene moiety that can be electrochemically switched (Table 3).[105] The difference between electron rich and poor state concerning their TEP values is greater than 10 cm^{-1} in both cases.

Table 3. Selected NHC systems featuring switchable donor strengths with their corresponding TEP values calculated with the aid of the formula by Glorius *et al.*[9d] based on the IR data of the respective [IrCl(CO)$_2$(NHC)] complexes.[105-106]

electron rich state	**I-94** (2048.2 cm^{-1})	**I-95** (2049.8 cm^{-1})	**I-96** (2049.8 cm^{-1})	**I-97** (2044.9 cm^{-1})
electron poor state	**I-94*** (2060.9 cm^{-1})	**I-95*** (2060.9 cm^{-1})	**I-96*** (2055.8 cm^{-1})	**I-97*** (2058.9 cm^{-1})
Δ(TEP)	12.7 cm^{-1}	11.1 cm^{-1}	6.0 cm^{-1}	14.0 cm^{-1}
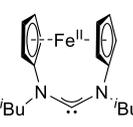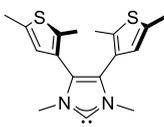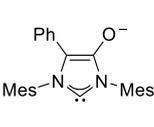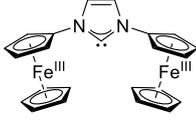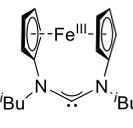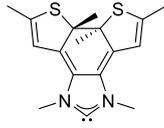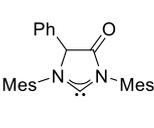
Bielawski and co-workers coordinated the photoswitchable ligand **I-96** developed by Yam *et al.*[107] to an iridium center and could show that upon UV-irradiation a reversible C–C bond formation and cleavage between the proximal thiophene entities in the ligand's backbone is caused.[106b] Subsequently, this ligand system was successfully employed as photoswitchable organocatalyst.[108] Another example by Glorius *et al.* is based on the introduction of a carbonyl functional group into the ligand backbone resulting in the rather electron poor ligand **I-97***.[106a] Upon deprotonation of the carbon atom in α-position of the C=O moiety an enolate is formed leading to the particularly electron rich system **I-97**. Another structural motif applicable to this chemistry comprises of quinone-related ligands, one of which was tested for its redox chemistry and in switchable Kumada cross-coupling transformations.[34]

2.4 Steric Properties

Homogeneous catalysis with metal complexes has become a striving and versatile field of research, both in academia and industry.[109] For that, the thorough fine-tuning of the ligand(s) coordinated to the catalyst is an operation that is critical to success. For spectator ligands, such as phosphines, or *N*-heterocyclic carbenes the steric demand plays a crucial role in virtually all catalytic applications which they are used for. Exemplarily, reports by Glorius *et al.*, as well as Organ *et al.* showed that steric properties of the carbene ligands are the key handle for the optimization of catalytic activity in C–C bond formation reactions catalyzed by palladium NHC complexes.[110] In general, the fine-tuned steric bulk around the catalytically active metal center governs its substrate selectivity and oftentimes is a prerequisite for specific transformations to proceed. Also, during the synthesis of coordination compounds the steric demand of the ligand(s) involved heavily influences the structural outcome.[59]

Thus, early efforts were made to establish a reliable measure for steric dimensions of phosphines and later NHCs. Tolman was the first to propose the concept of the cone angle θ defined with the metal at the vertex and the atoms at the perimeter of the cone (Figure 16, left).[92] For that, space-filling models with a metal to phosphorus distance of 2.28 Å (standard Ni–P bond length in [Ni(CO)$_3$L]-type complexes) were employed. The model was initially designed for tertiary phosphine ligands, but is theoretically applicable to any given ligand. However, owing to more recent development of structurally more sophisticated compounds, such as biarylphosphines (Buchwald ligands),[111] multidentate systems,[112] and especially *N*-heterocyclic carbenes,[9a] steric parameter calculations *via* the Tolman model have proven difficult and oftentimes resulted in inappropriate values.
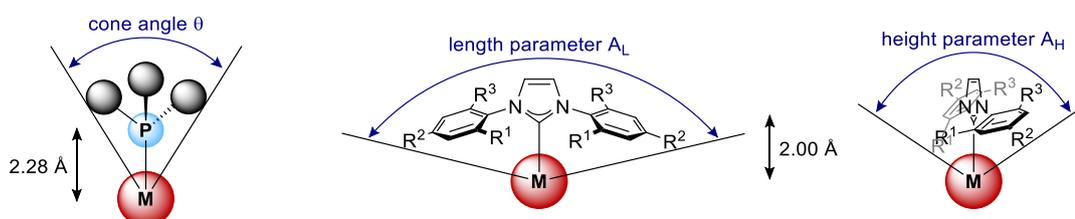

Figure 16.   The Tolman cone angle θ developed for phosphine ligands (left), and derived model for steric parameter determination of NHCs proposed by Nolan.[113]

For a better assessment of the steric demand of NHCs, an early model based on crystallographic data derived from Tolman's system was presented by Nolan and co-workers.[114] Instead of taking into account the cone angle exclusively, two values are calculated to cope with the anisotropically distributed bulk of NHCs, namely the length parameter A_L (Figure 16, middle), as well as the height parameter A_H (Figure 16, right). In the first report,[114] the metal carbene bond distance was set to 2.105 Å, but later harmonized to 2.00 Å as an average value.[113] In order to validate the model a steric versus enthalpic relationship was established and provided a fair correlation. However, this first simple method soon reached its limits calling for an improved metric parameter for steric bulk for this ligand family.

Subsequently, Nolan, Cavallo and co-workers proposed a different model to define the steric bulk brought about by NHC ligands that relies on the evaluation of the "percent buried value" (% V_{bur}) defined as the percentage of the total volume of a sphere occupied by a ligand (Figure 17).[87a] The hypothetical sphere has a given radius and has the metal center at the core. Typically, % V_{bur} is calculated from ligand coordinates extracted from the crystal structure of the respective transition metal complex of interest. It is important to note for comparison of the obtained data, that identical NHC ligands can adopt slightly differing buried volumes depending on the metal center, as well as the number and type of remaining ligands coordinated to it.
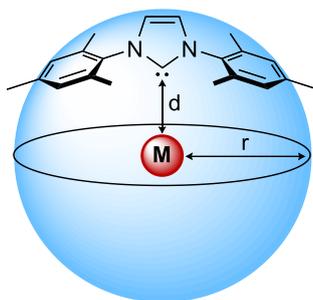

Figure 17. Schematic representation of the model for 'Percent Buried Volume' calculations by the web application "SambVca" reported by Cavallo and co-workers (d = M–NHC distance, r = sphere radius).[115]

Thus, Cavallo *et al.* proposed to employ quantum chemically optimized ligand geometries obtained from the respective computed [IrCl(CO)$_2$(NHC)]-type complexes that are utilized frequently for the determination of TEP data as well.[115] In the same report, the group introduced the user-friendly web-based software "SambVca" (**Sa**lerno **m**olecular **b**uried **v**olume **ca**lculation) allowing researchers to obtain spatial occupation values of ligands in a very straightforward manner after uploading geometrical data derived from crystallographic or computational data of the corresponding (novel) ligand entities. Originally, the application was developed specifically for NHCs, exemplarily shown for carbene complexes featuring ruthenium,[87a] iridium,[93b] palladium,[116] rhodium,[117] nickel,[44] gold,[118] and silver,[119] but in principle it can be applied to all sorts of other coordination chemistry ligands. For data comparability reasons it is advisable to use identical parameters for atomic radii, sphere radius and metal to ligand distance based on the iridium model compounds. Apart from the most commonly employed NHCs, some of which are listed in Figure 18 with their corresponding buried volume, examples for more exotic ligand motifs with exceptionally high % V_{bur} values have been synthesized. One example is the cyclic alkyl amino carbene (CAAC) scaffold **I-79** reported by Bertrand and co-workers (% V_{bur} = 51.2 %, Figure 18),[120] or dioxazoline-based ligand motifs with buried volumes up to 47.7 %.[9d,110a]

| **I-40** | **I-98** | **I-26** | **I-99** | **I-48** | **I-78** |
| % V_{bur} = 24.9 % | % V_{bur} = 30.5 % | % V_{bur} = 31.6 % | % V_{bur} = 35.5 % | % V_{bur} = 36.1 % | % V_{bur} = 57.3 % |
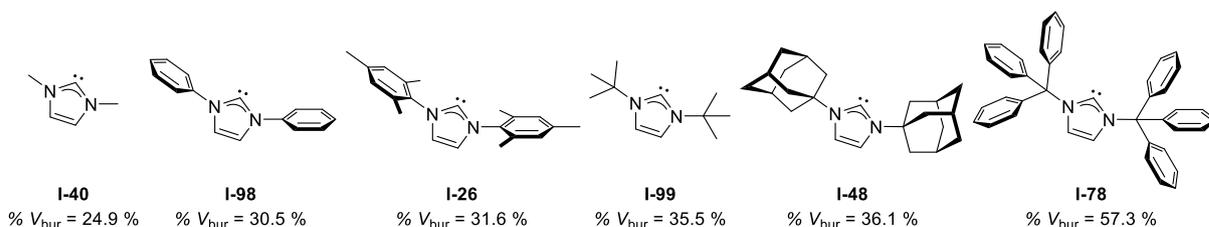
Figure 18. Examples of common NHC ligands with their percent buried volume (% V_{bur}), as calculated by Cavallo *et al.* with "SambVca" application (atom radii = 1.17 Å, sphere radius = 3.5 Å, M–NHC distance = 2.10 Å).[115]

Very recently, Rivard *et al.* presented the extremely crowded trityl-substituted ligand **I-78** featuring the highest buried volume value to date (% V_{bur} = 57.3 %, Figure 18).[121] Consequently, they showed that these systems are suitable for the stabilization of low-valent inorganic cations. As the % V_{bur} concept completely neglects substrate interactions, the model is not applicable for predicting the outcome of catalytic transformations. Thus, more elaborated quantum chemical techniques need to be taken into consideration for such investigations.[122]

2.5   Macrocyclic NHC complexes

2.5.1 From Porphyrins to macrocyclic NHCs

Macrocyclic ligands are defined as compounds that form a continuous ring around a metal center and consist of at least nine ring atoms, three of which are potential donor atoms. They have been shown to form extremely robust complexes due to the macrocyclic effect.[123] The most prominent class among these ligands is without doubt that of porphyrin systems as they play a crucial role in biological systems and have widespread applications either as free porphyrins or metallaporphyrins (Figure 19).[124] Porphyrins describe one group of vital chemical compounds essential for life processes on earth. A multitude of enzymes contain a porphyrin core as prosthetic group, such as chlorophylls that perform photosynthesis, heme as a component of hemoglobin responsible for the oxygen transport to animal tissues as well as myoglobin that transports oxygen in a cell.[124a-c] Due to their utmost importance in biologic systems, a lot of research has been conducted on these compounds and allowed for a substantial understanding of the structure-function relationship of natural occurring porphyrins enabling the design of simplified test systems for chemical, physical and biological investigations.[125] Synthetic porphyrins and their metalladerivatives have been studied widely and intensely in the area of catalysis and mimicking enzymes, such as catalase and peroxidase.[126] Furthermore, they gained importance as NMR image enhancement agents,[124e] nonlinear optical materials,[124f] and DNA binding or cleavage agents.[124d,124g]
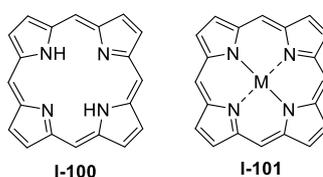

Figure 19.   Porphin (**I-100**) and corresponding metallaporphin **I-101**.

Porphyrins are cyclic tetrapyrrole derivatives with a highly delocalized planar π-framework. The parent compound of this group of macrocycles is porphin (**I-100**) with the chemical formula $C_{20}H_{14}N_4$ consisting of four pyrrole rings joined together by four methine groups. Around the perimeter of the macrocyclic ring, there is a cyclic chain of 20 sp^2 hybridized carbon atoms, all of which are part of a conjugated double bond system. Since they are 26-π electron systems, porphyrins fulfill the requirement for Hückel aromatics (4n+2 π-electrons).[127]

The porphyrin ring provides a vacant site at its center, ideally suited for metal incorporation. As the two protons at the nitrogen atoms of the pyrrole rings opposite to each other possess acidic

character (pK_a ≈ 16)[128] they can easily be deprotonated to give the respective porphyrinato ions that exhibit remarkable ligation capabilities towards metal ions. Hence, derivatives of porphyrins with a huge variety of metals and semimetals have been synthesized and studied in detail.[124b] A crucial factor for the formation of such complexes is the compatibility of the porphyrin ring size with the ionic radii of the metal cations.[129] The tetrapyrrole network gives rise to a square planar coordination sphere around the metal atom resulting in a minimal coordination number of four. Further ligation of the central ion by additional monodentate moieties results in square pyramidal or octahedral complexes, respectively. The nature of bonding between a metal atom and the porphyrin ligand essentially originates from the presence of two different types of nitrogen donor atoms: two "classical pyridine" type ligands (σ-donor and π-acceptor) and two "unusual" amide-*N*-ligands (σ- and π-donor).[130] Therefore, electron rich metals can be stabilized due to the π-acceptor character of the amine-type sites, whereas electron poor metals (in high oxidation states) can also be stabilized *via* electron donation from the amide sites of the ligand.

The formal exchange of the heterocyclic building units of the macrocycle from pyrroles to *N*-alkylated imidazoles results in potential NHC ligand precursors as the resulting donor atom in each heterocycle would be a carbon atom framed by two nitrogen neighbors (Scheme 18). Macrocyclic tetradentate carbenes with bridging methylene groups would be structurally similar to, but electronically fundamentally distinct from the porphyrin systems, from which metal complexes with interesting properties may arise.[131] As carbon is softer and less electronegative than most heteroatom Lewis bases, metal-to-ligand backbonding in NHC complexes is comparatively weak,[47] a different bonding situation may be expected for these calix[4]imidazolylidene-based ligands in comparison to their porphyrin analogues. Additionally, polydentate NHC ligands lack delocalized scaffolds, because the *N*-wingtips usually contain one or more saturated bridging moieties. In principle, also extended porphyrin-based scaffolds, such as the Siamese-twin porphyrin **I-104** by Meyer *et al.* could serve as structural template for macrocyclic NHC ligands (Scheme 18).[132]
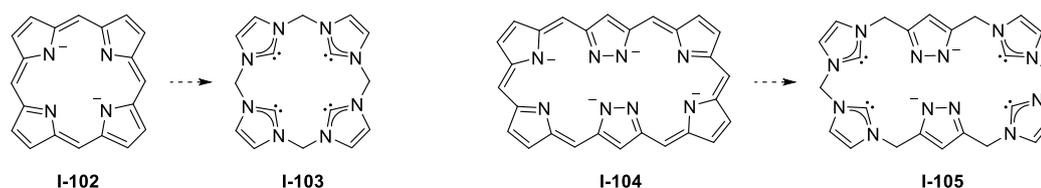

Scheme 18.   The standard as well as the Siamese-twin porphyrinato frameworks **I-102** and **I-104** as structural templates for macrocyclic tetra(NHC) ligands.[132-133]

However, the area of macrocyclic NHC compounds is relatively young and scarcely investigated, mostly due to their challenging and lengthy syntheses as compared to their acyclic analogues. To date, two synthetic approaches for the formation of macrocyclic ligands that incorporate NHC donor groups exist. The first strategy consists of an on-site strategy, that relies on the preparation of properly functionalized, monodentate NHC moieties at a suitable metal template followed by connection of the ligands coordinated to the template center to form polydentate macrocycles.[134] The second, more generally applicable method is the synthesis of macrocyclic poly(azolium) salts followed by their deprotonation to the poly(NHC) derivatives.

2.5.2 Template synthesis of poly(NHC) macrocycles

Early reports by Fehlhammer *et al.* showed that it is possible to access heterocyclic carbenes from 2-hydroxyalkyl isocyanides *via* a 1,2-addition across the C≡N triple bond. Coordination of the isocyanide to an electron-poor metal center initiates the spontaneous intramolecular cyclization to an oxazolidin-2-ylidene ligand.[135] Utilizing this methodology, homoleptic tetra-[136] and hexa-NHC complexes[137] could be synthesized. Upon (post-)modification of compounds obtained *via* this route, a great variety of NH,O- and NR,O-functionalized carbene ligands have been prepared.[138] Based on these results Hahn and co-workers were able to extend this motif to NH,NH-NHC ligands by employing 2-azidophenyl isocyanides as synthons for the unstable 2-aminophenyl isocyanide.[139] Upon addition of trialkyl phosphines to the metal-coordinating 2-azidophenyl isocyanide a Staudinger reaction occurs and after hydrolysis of the formed phosphinimine to the primary amine an intramolecular ring closing reaction affords the respective NHC ligated complex, such as **I-106** (Scheme 19).
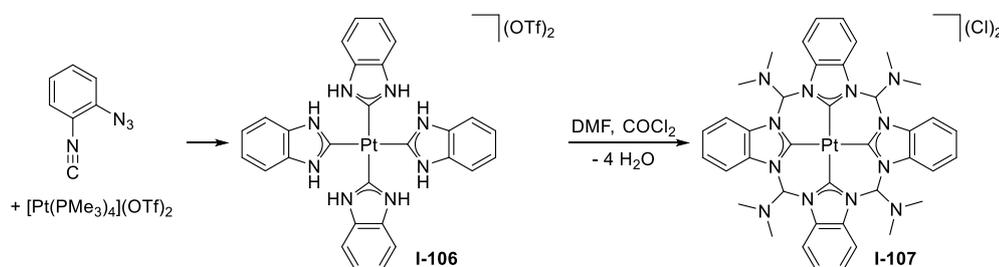
Scheme 19.   Template synthesis of macrocyclic complex **I-107** *via* cyclization of **I-106**.[140]

Coordinated NH,NH-NHCs are very useful building blocks because of the preservation of the nucleophilic reactivity at the nitrogen atoms in the heterocycle. Four of these ligands bound to a square planarly coordinated metal center, such as Pt[II], are ideally preorganized for a subsequent interconnection of the individual heterocycles to a single macrocyclic tetra(carbene) ligand *via* bridging *N,N'*-dialkylation with a suitable spacer. Hahn *et al.* were able to synthesize compound **I-107** containing a cyclic tetra(carbene) ligand with a crown ether topology from **I-106** in dimethyl formamide in the presence of phosgene.[140] Employing a similar template-assisted strategy, Hahn and co-workers prepared a planar [16]ane-P$_2$C$^{NHC}_2$ macrocyclic ligand.[141] The reaction of *trans*-di(carbene) complexes of the type **I-108** with phenyldivinyl phosphine in dimethyl formamide afforded **I-109**. The facile template controlled macrocycle formation proceeds *via* a fourfold hydroamination reaction without additives (Scheme 20).
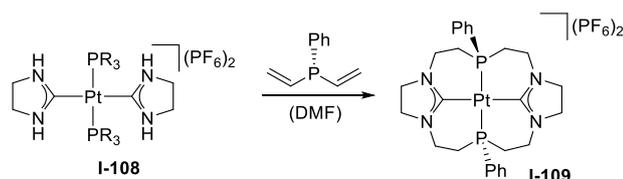
Scheme 20.   Reaction of complex **I-108** with phenyldivinyl phosphine under formation of **I-109**.

Another subgroup of macrocyclic ligands feasible *via* template synthesis is the [11]ane-P$_2$C^{NHC}. In analogy to reactions where a nucleophilic attack of coordinated phosphides at coordinated *ortho*-fluorophenyl diphosphines is utilized as versatile and facile route to P–C bond formation,[142]

this method utilizes the fluoride displacement reaction by nitrogen nucleophiles for forming N–C bonds. As starting material for the macrocyclization complexes such as **I-110** are applicable. Addition of a base to **I-110** leads to deprotonation of the NHC ligand and an intramolecular nucleophilic attack of the nitrogen atoms at two proximal C–F bonds of the phenyl substituents to yield **I-111** (Scheme 21).[143] The analogous reaction sequence was successfully applied to the respective manganese complex.[144] A disadvantage of the template-strategy, as was encountered during this study, is the instance, that the newly formed macrocycle cannot be liberated from the metal center without decomposition.[134] The on-site synthesis of [11]ane-P$_2$C^{NHC} was then accomplished at ruthenium[145] as well as iron centers.[146] In both cases the reaction sequence is very delicate in terms of suitable metal precursors.
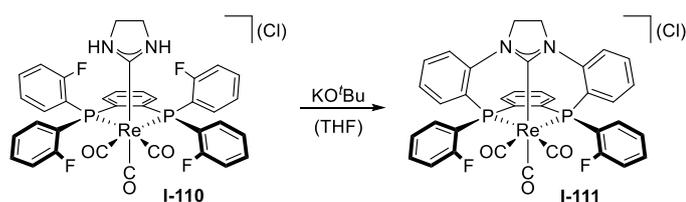
Scheme 21. Template synthesis of the [11]ane-P$_2$C^{NHC} macrocycle at a Re center during the formation of **I-111** from **I-110**.[143]

To summarize, the template approach is a very elegant way for the synthesis of macrocyclic *N*-heterocyclic ligands and enables the formation of frameworks that would otherwise not be feasible. On the contrary, this strategy is very limited in its scope, as only a handful of compounds come into consideration for their synthesis. Furthermore, a liberation of the bound macrocycles proves to be problematic.

2.5.3 Poly(NHC) ligands from macrocyclic poly(azolium) precursors

Compounds that contain imidazolium moieties have been recognized as potent anion receptors early on.[147] In contrast to ammonium-based receptors, these compounds are stable both in acidic and basic media, which renders them more versatile receptors for various conditions.[148] The cationic group is capable of forming distinct interactions with anions through (C–H)$^+$···X$^-$ type hydrogen bonds.[149] Initially, tripodal[149-150] and other acyclic derivatives[151] were heavily employed for this purpose. Simultaneously, the first macrocyclic cyclophanes and calix-imidazolium systems were introduced and showed superior affinities towards various anions (Figure 20).[30,152]


I-112a (n = 1)
I-112b (n = 2)

I-113
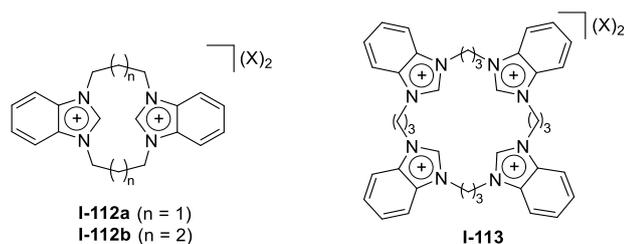
**Figure 20.** First macrocyclic compounds based on interlinked imidazolium heterocycles.[153]

The first macrocyclic imidazolium compounds were reported already half a decade earlier by Thummel and co-workers,[153] however, their anion binding capability was not examined (Figure 20). Since its origins in the mid 1990s, the field of anion recognition with macrocyclic imidazolium-based scaffolds has become a striving field of research.[30,154]

Apart from anion recognition in solution these macrocyclic poly(azolium) salts are also potential NHC ligand precursors. Consequently, the first studies applying these systems in metalation reactions surfaced shortly after.[155] The benzimidazolium derivatives **I-112a** and **I-112b** as well as a number of structurally related compounds with different linkers between the azolium moieties are generally not capable of forming the corresponding macrocyclic carbene complexes. As they only contain two donor sites that normally occupy *cis*-positions after C2 deprotonation they tend to form MLX_2-type products and act as classical bidentate ligands rather than encapsulating the metal in a manner typical for macrocyclic ligands.[155b] Metal ions that prefer a linear coordination lead to binuclear complexes of the motif M_2L_2.[155a] In both cases the metal is not bound in the center of the macrocycle. The first true macrocyclic NHC complex with four donor sites in the ligand was synthesized by Baker *et al. via* reaction of the bis(imidazolium) salt **I-114** with nickel(II) acetate (Scheme 22). After abstraction of the two C2 protons of the imidazolium cations by the internal base of the metal precursor and subsequent coordination of the resulting macrocyclic di(carbene) ligand to the Ni^{2+} ion, complex **I-115** was obtained.[155c]
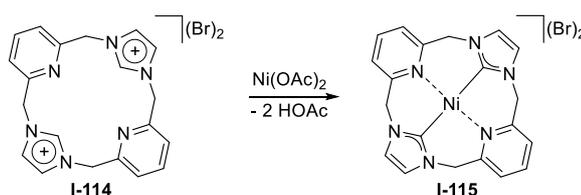
Scheme 22. First macrocyclic NHC complex **I-115** synthesized from precursor **I-114**.[155c]

This initial report sparked the activity in this field and in the following years a variety of macrocyclic imidazolium salts were prepared and employed for the synthesis of the respective transition metal NHC complexes with different metal centers, such as copper, silver, cobalt or palladium.[156] Later, the first asymmetrically bridged macrocycles, such as tetra(imidazolium) salt **I-116** were reported by Jenkins and co-workers (Scheme 23).[29a]
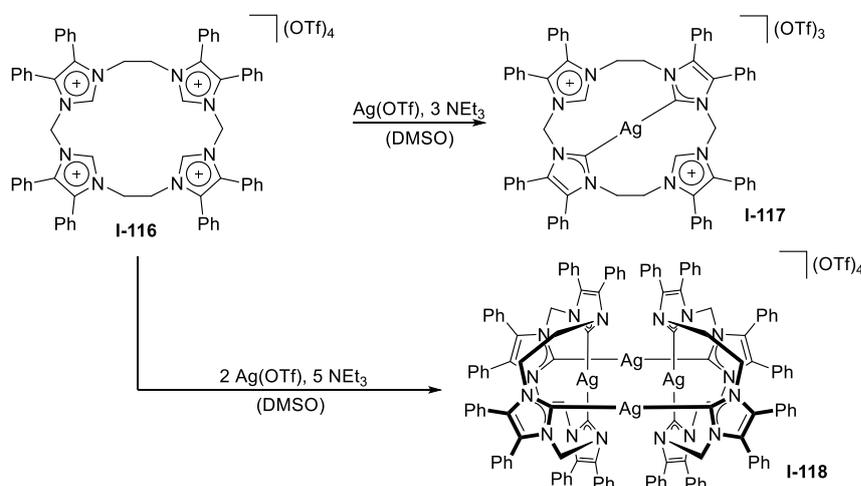

Scheme 23. Asymmetrically bridged proligand **I-116** and the respective silver complexes **I-117** and **I-118**.[157]

They were able to show that it is possible to only partially deprotonate the imidazolium moieties in the macrocycle by adjusting the amount of silver(I) precursor.[157] Thus, complex **I-117** was obtained when employing a 1:1 ratio of ligand precursor to Ag(OTf), whereas the tetranuclear compound **I-118** resulted as product when setting the ratio of macrocyclic precursor to silver triflate to 1:2. The dimeric complex **I-118** was used as transmetalation reagent to synthesize macrocyclic tetra(carbene) complexes with a variety of different metals, such as Pt[II], Rh[III], Co[II] and Ru[II]. Additionally, a potential intermediate of the transmetalation reaction was isolated and characterized, suggesting that carbene bonds to inter-macrocycle silver(I) centers of **I-118** are the first ones to break upon formation of the novel M–C bonds.

Spicer, Tuttle, Murphy and co-workers were the first to use a macrocyclic poly(imidazolylidene) complex for catalytic applications.[158] They prepared a crown-tetra(carbene) nickel(II) compound featuring a ligand scaffold with propyl-bridges between each *N*-heterocycle, that was earlier reported by the same group.[156a] Subsequently, they reduced the complex to a formal Ni[0] entity with Na/Hg and applied the resulting species successfully for the reduction of challenging substrates. The reduced complex is able to reductively cleave arenesulfonamides, including those derived from secondary aliphatic amines, and effect Birch reduction of anthracenes as well as reductive cleavage of stilbene oxides. Computational studies revealed that the orbital that receives electrons upon reduction of the complex is predominantly based on the crown carbene ligand suggesting redox non-innocent behavior.[156a]

Jenkins *et al.* demonstrated that also heteroatoms can readily be used as bridging entities in poly(imidazolium) cyclophanes by synthesizing the macrocyclic tetra(imidazolium) diborate proligand **I-119** capable of forming dianionic NHC ligands due to the negative charge on each borate center (Scheme 24).[159]
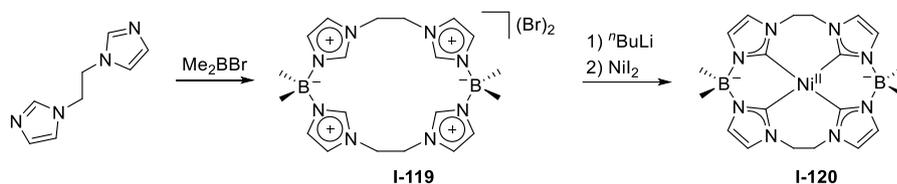

Scheme 24. Synthesis of neutral NHC complexes of type **I-120** based on the macrocyclic tetra(imidazolium) diborate proligand **I-119**.[159]

Deprotonation of the precursor salt **I-119** with *n*-butyllithium followed by the addition of divalent metal halides of palladium or nickel led to macrocyclic tetra(carbene) complexes of type **I-120** with an 18-atom macrocycle. These neutral NHC complexes are the first examples of macrocyclic tetra(carbene) diborate complexes, and unlike their cationic counterparts, they exhibit a high solubility in non-polar solvents.

The iron complexes featuring the ligand scaffolds **I-116** and **I-119** were found to be active catalysts for azidirination reactions of particularly challenging substrates.[160] Important contributions to the chemistry of macrocyclic imidazolium salts were also made by Hahn *et al.* by introducing numerous macrocyclic proligands and their subsequent transition metal complexes.[161] Especially, the silver(I) NHC complexes reported by this group are highly interesting systems due to the uncommon structural motifs and transmetalation properties they exhibit.[161b,161c,162]

More recently, tetra(carbenes) were repeatedly used for the synthesis of several macrocyclic iron(II) complexes that were then studied for their reactivity towards small molecules and capability to act as catalysts in oxidation reactions. The first important milestone for this purpose was achieved by Meyer *et al.* by isolating the iron(IV) oxo complex **I-122** stabilized by a tetra(NHC) ligand as first example of a $Fe^{IV}=O$ moiety that is not supported by an oligodentate *N*-donor ligand, but an organometallic scaffold (Scheme 25, bottom right).[163] Such Fe^{IV} species are key intermediates in the catalytic cycles of numerous heme and non-heme iron enzymes that insert an oxygen atom from dioxygen into unactivated C–H bonds.[164] Upon treatment of **I-121** with an excess of a iodosylbenzene derivative the oxoiron(IV) complex **I-122** was obtained, whereas the μ-oxo diferric complex **I-123** formed from **I-121** by oxidation with *m*CPBA, *N*-oxides, or aerial O_2.
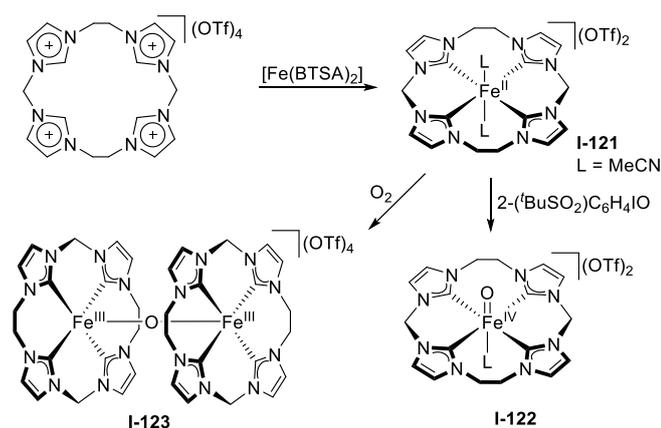
Scheme 25. Synthesis of the macrocyclic Fe^{II} NHC complex **I-121** and its oxidative transformations to the Fe^{IV} oxo complex **I-122**, as well as the μ-oxo diferric compound **I-123**.[163]

Based on this report, the reactivity of iron(II) complexes of this type towards nitric oxide, carbon monoxide and other substrates was studied.[29b,165] The FeNO tetra(carbene) complex was shown to exhibit rather unusual structural and spectroscopic signatures that suggested Fe^INO^+ character to a certain extent.[29b,165] Inspired by these properties, Meyer *et al.* were then able to access a complete series of FeNO complexes stabilized by this tetra(carbene) macrocycle in different oxidation states by reduction with $CoCp_2$ and oxidation with O_2, respectively.[166]

Simultaneously, the group of Kühn tested similar Fe^{II} and Fe^{III} complexes with methylene-bridged tetra(NHC) ligands for their reactivity towards oxygen and their application as homogeneous catalysts for epoxidation reactions of olefins.[167] The complexes showed exceptionally high activities of up to 183000 turnovers per hour at room temperature and turnover numbers of up to 4300 at -30 °C. For the Fe^{III} complex, a decreased Fenton-type reactivity was observed compared to Fe^{II} catalysts reported previously,[168] leading to a substantially lower H_2O_2 decomposition and higher (initial) turnover frequencies.

This tremendously fast development from the first macrocyclic NHC complexes to highly elaborated architectures for applications in catalysis and small molecule activation certainly highlights the impact and future potential of this ligand class.

2.6 Pyrazolato-bridged NHC complexes

There has been considerable interest in bi- and multimetallic transition metal complexes due to potential metal-metal cooperative phenomena as found in a variety of metal-biosites.[169] Hence, the attempt to establish distinct reactivity patterns based on the cooperation between two metal centers in model complexes is a promising research target with great future potential. This objective requires the design of appropriate ligand systems providing coordination sites with well-defined metal-metal separations. The ability of the diazine unit of pyrazolates to bridge two metal ions is well known.[170] Thus, much effort has been put into the synthesis and characterization of binuclear complexes utilizing this bridging motif, especially with pyrazole entities bearing additional donor groups in the 3- and 5-positions of the heterocycle in order to design two appropriate binding pockets for the coordination of the desired metal centers.[171]

Early efforts by Schenck *et al.* provided a useful and large-scale synthetic access to the dichlorinated 3,5-dimethylpyrazolium chloride **I-124** that is suitable for further modifications by simple substitution of the chlorides by nucleophiles such as phosphines.[172] As this difunctionalized pyrazole is prone to side reactions, such as oligomerization due to intermolecular substitution of the benzylic-like activated halides by the pyrazole's nucleophilic NH-group, Meyer *et al.* reported the synthesis of the *N*-protected 3,5-substituted pyrazoles **I-125** to circumvent this intrinsic problem (Figure 21).[171b,171c]


I-124

I-125, X = Cl, Br
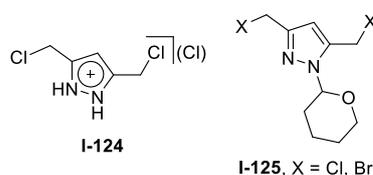
Figure 21. Functionalized 3,5-dimethylpyrazoles **I-124** and **I-125** suitable for further derivatization.[171b,171c,172]

With the aid of these precursors many different donor groups have been introduced successfully into the pyrazole system and subsequently used for the coordination of metal ions.[173] Zhou *et al.* were the first to expand this chemistry to ligands comprising *N*-heterocyclic carbene donor sites.[174] It was shown, that by deprotonation of **I-124** with the non-nucleophilic base silver(I) oxide and subsequent reaction of the corresponding neutral pyrazole building unit with a huge excess of *N*-methylimidazole, the pyrazole-bridged bis(imidazolium) salt **I-126** is generated after anion exchange to hexafluorophosphate.[174] Reacting **I-126** with silver(I) oxide yielded the tetranuclear silver complex **I-127** (Scheme 26, bottom right) supported by two of the pyrazole-linked di(*N*-heterocyclic carbene) ligands independent of the **I-126**/Ag$_2$O ratio.[174] The corresponding Au$_4$ complex **I-128** was synthesized by reacting **I-127** as transmetalation agent with the precursor [AuCl(SEt$_2$)]. Attempts to prepare an AgAu mixed cluster by changing the ratio of **I-127** and [AuCl(SEt$_2$)] were not successful, and workup only resulted in **I-128** and unreacted **I-127**. Both complexes exhibit a good stability towards air and moisture.[174] The three complexes **I-129**, **I-130** as well as **I-131** were synthesized by *in situ* transmetalation with Ag$_2$O.[175] This route turned out to be generally more applicable, whereas a direct one-pot reaction of **I-126** and metal precursor under Brønsted-basic conditions failed in certain cases.[175a,175b] The metal precursor used for the reaction has a major influence on the structure of the complex formed. When employing

[Ni(PPh$_3$)$_2$Cl$_2$], the formation of the Ni$_2$L$_2$-type product **I-129** was observed,[175b] whereas when using [Pd(allyl)Cl]$_2$, the resulting ratio of ligand to metal is 1:2, because the allyl moiety is not cleaved off, yielding complex **I-130**.[175a] In the case of ruthenium the product **I-131** was found to consist of Ru$_2$LCl units with additional acetonitrile coordinated to the metals to saturate their coordination spheres.[175c]
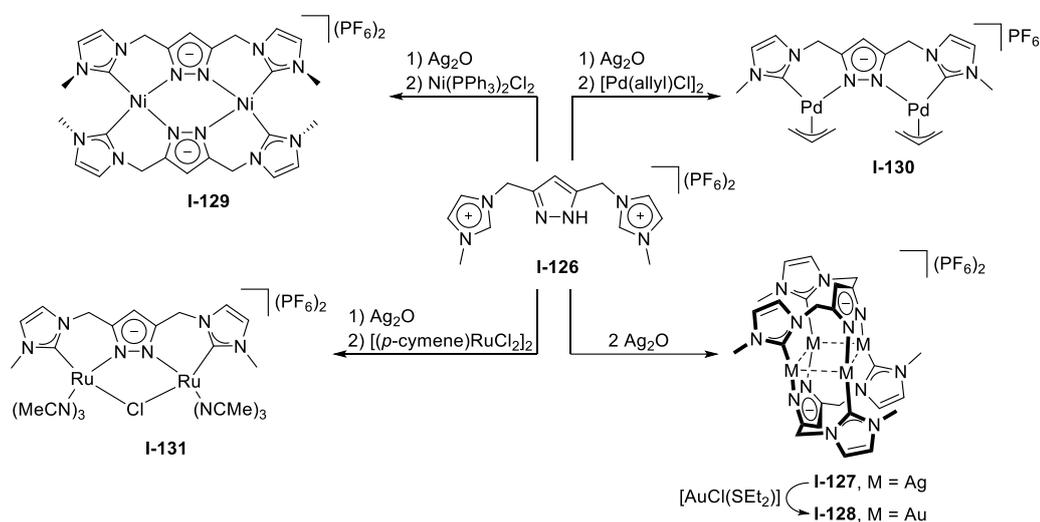
Scheme 26. Pyrazole-bridged ligand precursor **I-126** and deduced metal complexes **I-127**-**I-131**.[174-175]

Additionally, varying the wingtip substituents of the imidazole rings is achieved easily by employing different *N*-substituted imidazoles during the proligand synthesis. Accordingly, Meyer *et al.* reported that exchanging the methyl-wingtips in **I-126** with bulkier substituents, such as mesityl or diisopropylphenyl, instead of the tetranuclear complex **I-127** an octanuclear, tetrameric, "double-crown"-like product is obtained.[176] Zhou and co-workers synthesized binuclear nickel(II) complexes with ligands featuring different wingtips (methyl, picolyl and 2-pyridyl).[175b] The respective imidazolium salts caused different coordination patterns depending on their steric demand or the presence of additional donor groups. In the case of methyl, complex **I-129**, was formed, whereas for picolyl and 2-pyridyl the binuclear products **I-132** and **I-133** with a ligand/Ni ratio of 1:2 were found (Scheme 27).
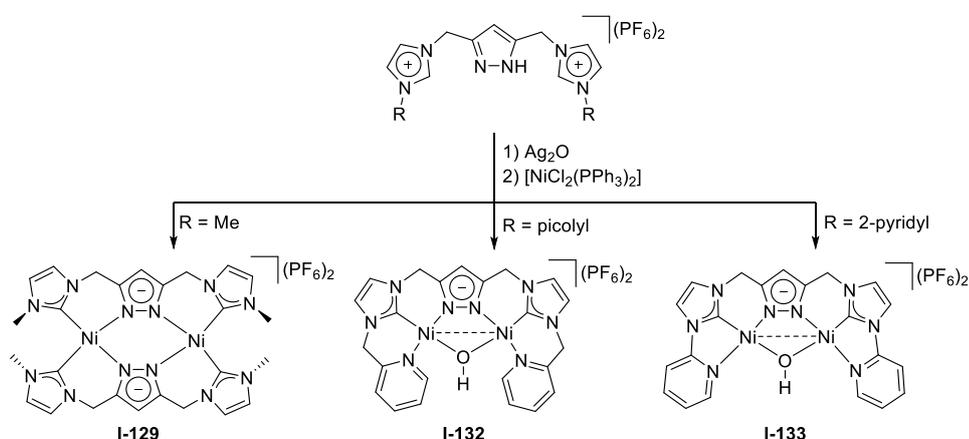
Scheme 27. Dimetallic nickel NHC complexes **I-129**, **I-132** and **I-133** accessible by employing ligand precursors with various wingtips.[175b]

These products are favored over a Ni₂L₂-type complex due to the *N*-donors in an adequate distance to coordinate the metal atoms in a way that each nickel atom exhibits an N–C–N-coordination provided by the ligand plus a μ-hydroxo group originating from Ag₂O to saturate the square planar coordination sphere of the Ni atoms. Nickel(II) complexes bearing *N*-heterocyclic carbenes are known to act as convenient catalyst precursors for C–C-coupling reactions, as the active species can be generated *in situ* in the presence of bases or reactants. Under Suzuki-Miyaura conditions, Ni^{II} is reduced to Ni^{0} by the substrate (arylboronic acid) *via* a Pd^{II}-related mechanism.[177] Thus, the complexes **I-132** and **I-133** were tested in the coupling of aryl halides bearing electron-withdrawing and electron donating substituents under typical reaction conditions commonly applied for nickel-catalyzed Suzuki reactions,[178] and indeed found to be very active catalysts.[175b]

More recently, Herrmann *et al.* studied Ru^{II} and Rh^{III} complexes bearing the pyrazolato-bridged bis(imidazolium) moiety and showed that the ligand has two possible modes to form a binuclear complex depending on the reaction conditions applied (Scheme 28).[175c] Upon reaction between **I-121**, [(*p*-cymene)RuCl₂]₂ or [Cp*RhCl₂]₂ and Ag₂O in dichloromethane at room temperature, compounds **I-134** and **I-135** were obtained as the exclusive products. Even the addition of excess Ag₂O, only the pyrazole ring was deprotonated, whereas the imidazolium moieties remained unchanged. The di(NHC) complex **I-136** was formed in a direct manner using the same starting materials as for the synthesis of **I-134** at an elevated temperature of 110 °C. Complex **I-134** could be converted into **I-136** upon treatment with silver(I) oxide in acetonitrile at 110 °C.[175c] When applying analogous conditions for the synthesis of the respective Rh^{III} compound **I-137** employing [Cp*RhCl₂]₂ as a precursor, only mixtures of the di(NHC) complex **I-137** and the bis(imidazolium) complex **I-135** were isolated. The two compounds were separated conveniently, as **I-137** is soluble in dichloromethane, whereas **I-135** is not.

I-134, M = Ru; L = *p*-cymene
I-135, M = Rh; L = Cp*

I-136, M = Ru; L' = 3 CH₃CN
I-137, M = Rh; L' = Cp*
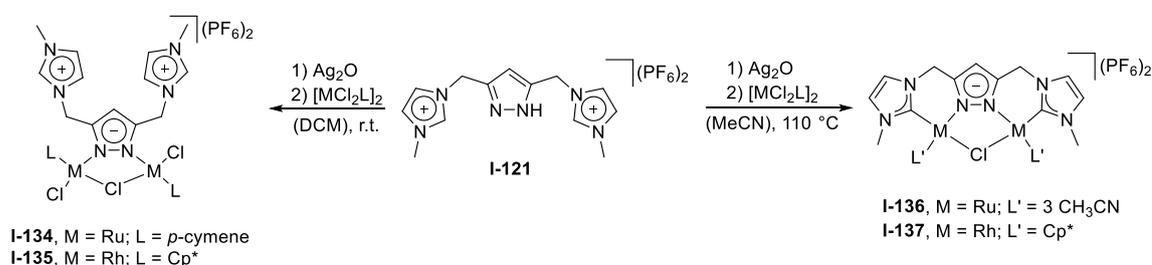
Scheme 28. Bimetallic Ru^{II} and Rh^{III} NHC complexes **I-134**-**I-137** obtained by variation of the reaction conditions. Low temperatures favor the formation of **I-134** and **I-135**, whereas elevated temperatures favor the formation of **I-136** and **I-137**, respectively.[175c]

In order to synthesize the di(NHC) complex **I-137** solely, first the silver complex **I-127** was synthesized and subsequently reacted with [Cp*RhCl₂]₂. In contrast, when aiming for the exclusive synthesis of **I-135**, it was shown that the reaction between the ligand precursor **I-121**, [Cp*RhCl₂]₂ and only 0.5 equivalents of Ag₂O solely yielded the desired bis(imidazolium) complex **I-135**.[175c]

Meyer *et al.* were the first to report binuclear palladium NHC complexes that feature abnormally coordinated NHC groups appended to the pyrazolate (Scheme 29).[179] They showed that the course of the reaction between pyrazole-bridged bis(imidazolium) proligands, such as **I-138** and Pd(OAc)$_2$ decisively depends on the amount of NH$_4$OAc present in the reaction mixture. In the absence of NH$_4$OAc products with abnormal NHC coordination (**I-139**) were formed, whereas addition of two equivalents of NH$_4$OAc selectively yielded the analogous complexes with normal NHC binding (**I-140**). This was attributed to a carboxylate-assisted reaction pathway for the formation of C2-bound (normal) NHC complexes.[179]
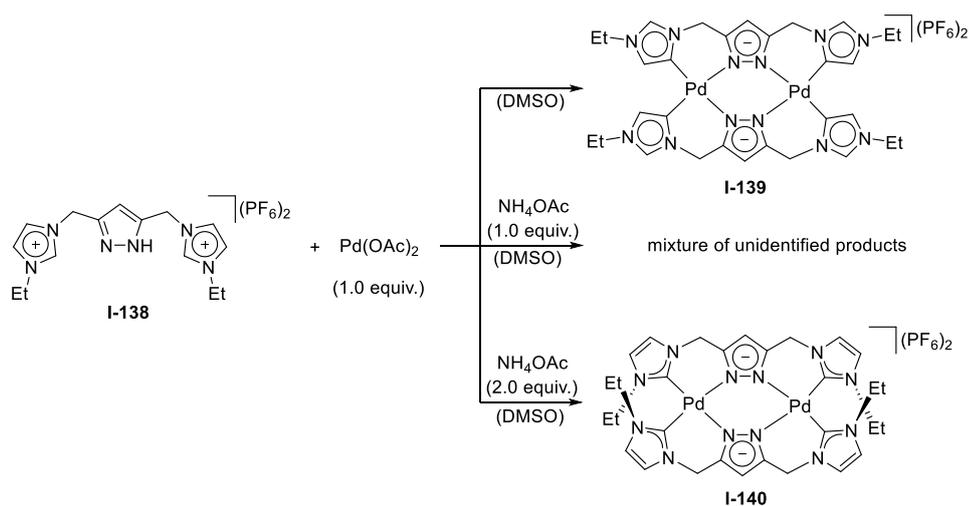
Scheme 29. Formation of the abnormal complex **I-139** and the normal complex **I-140** depending on the amount of NH$_4$OAc being present.[179]

2.7   Applications

The properties described beforehand render *N*-heterocyclic carbenes a highly valued and powerful class of ligands for a multitude of applications,[8b] a selection of which will be briefly described in this section (Scheme 30). The field of research which NHCs are employed in arguably most frequently, is that of homogeneous catalysis for organic transformations. After the discovery of their capability to act as viable spectator ligands for homogeneous catalysts with a broad range of adjustable features by Herrmann *et al.* in 1995,[5b] NHC ligands soon became an integral part of privileged catalysts for a manifold of processes for academic, but also for commercially relevant purposes. The topic is subject of several review articles and book chapters.[9a,9b,180]
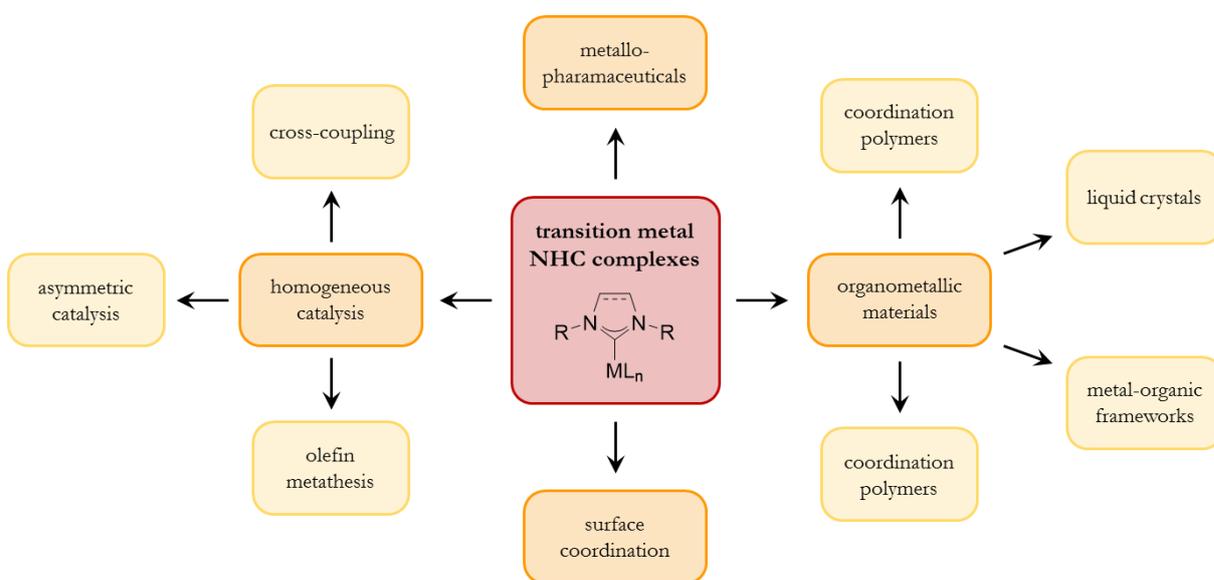
**Scheme 30.**   Graphical representation of the major applications of transition metal NHC complexes.[8e]

Amongst others, NHC complexes have been applied successfully in hydrogenation and hydrogen transfer reaction catalyzed by Ir and Ru compounds,[181] gold-catalyzed π-bond activation,[182] or hydrosilylation transformations mediated by Rh and Pt entities.[183] However, the by far most researched catalytic reactions are cross-coupling reactions, catalyzed predominantly by Pd complexes,[110,184] as well as ruthenium-catalyzed olefin metathesis.[185]
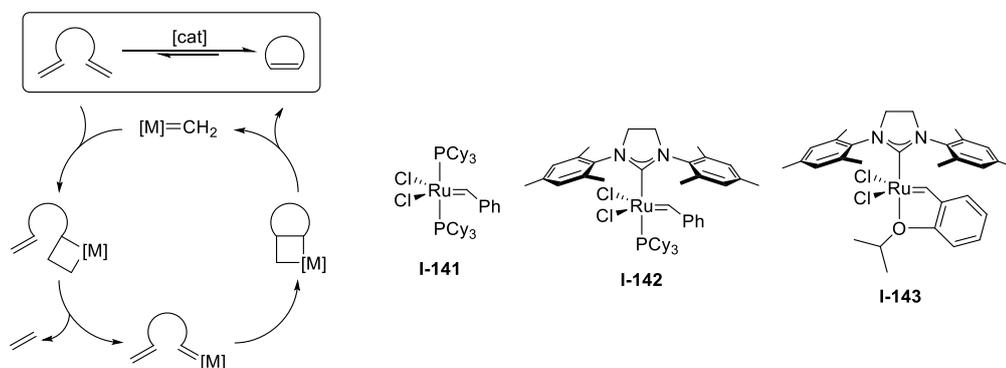
Scheme 31.   Left: General mechanism of the olefin metathesis, more specifically ring closing metathesis (RCM).[186] Right: Examples (**I-141**-**I-143**) of catalysts active in alkene metathesis.[69a,187]

One key feature of NHCs that renders them such powerful steering ligands, is increased catalyst stability, and consequently lower rates of catalyst decomposition resulting from strong metal ligand binding.[9a] The other factor is their extraordinary steric and electronic influence on the metal center causing an improved catalytic activity.[19] Benefitting from these properties, Grubbs and co-workers presented the nowadays most renowned NHC complex, namely the extremely efficient Grubbs' second-generation olefin metathesis catalyst **I-142** (Scheme 31).[185] Compared to its predecessor **I-141** (Scheme 31),[187a,187b] the first-generation congener featuring two phosphine ligands coordinated to the ruthenium center, compound **I-142** exhibits a significantly higher thermal stability whilst retaining its metathesis activity at substantially lower loadings. Additionally, the NHC complex is by far more reactive and at the same time tolerates a wider range of substrates with a variety of functional groups. Extensive mechanistic investigations revealed that the activity difference is caused by the relative substrate affinity after formation of the catalytically active 14 electron species by PCy$_3$ dissociation.[188] The initial binding of the coordinatively unsaturated metal center to the π-accepting olefin occurs with an affinity four times of magnitude larger for the NHC ligated catalyst **I-142** than for the phosphine analogue **I-141**. Subsequently, many further examples, amongst them the widely utilized Hoveyda-Grubbs catalyst **I-143** (Scheme 31),[187c,189] have been synthesized and applied for metathesis reactions. The impact of these transformations was honored with the Nobel Prize for chemistry in 2005.[190]

As mentioned above, the second major field of applications for complexes featuring *N*-heterocyclic carbenes as steering ligands is that of cross-coupling chemistry, that was likewise subject to the Nobel Prize five years later in 2010.[191] During the coupling reaction novel C–C and C–X bonds are formed catalyzed *via* a transition metal mediated cascade of oxidative addition, transmetalation and reductive elimination (Scheme 32). In this context, the beneficial electronic and steric properties of NHCs lead to an enhancement of the catalytic turnover of the substrates. First, the metal center is more prone towards oxidative addition into C–(pseudo)halogen bonds due to the strong σ-donating carbene donor. Thus, even challenging aryl chlorides with rather strong C–Cl bonds that generally suppress oxidative addition, can be activated by these catalysts. During the reductive elimination step the steric impact of the NHC on the complex supports the formation of the novel bond and the subsequent liberation of the product. Additionally, ligand-induced steric and electronic factors contribute to stabilizing the coordinatively unsaturated palladium(0) active species and hence reduce degradation of the catalyst to heterogeneous substances, such as palladium black, which is one of the main decomposition pathways.[8e]
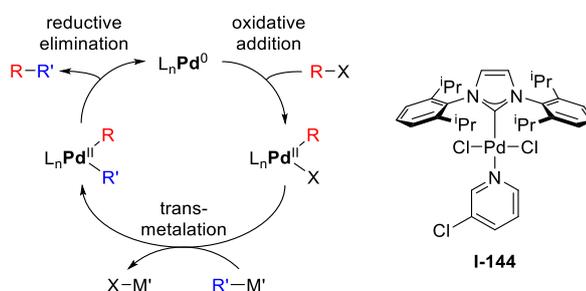
Scheme 32. Left: General mechanism of palladium-catalyzed cross-coupling reactions between organic halides and organometallic reagents (R, R' = aryl, heteroaryl, alkyl; X = (pseudo)halide; M = B(OR)$_2$, SnR$_3$, ZnR (also heteroatom coupling partners such as HNR$_2$).[184b] Right: Structure of the Pd-NHC pre-catalyst **I-144** active in cross-coupling reactions.[110b]

To date, a huge variety of NHC complexes has been synthesized and subsequently employed as extremely active and robust catalysts in a plethora of different coupling transformations. The vast majority of studies have focused on palladium-catalyzed processes,[110,184] but NHC complexes of other transition metals, such as nickel,[192] and iron,[193] have likewise been applied for this purpose and shown remarkable activities. In many modern catalytic procedures, the catalytically active NHC-metal complexes are generated *in situ* by mixing of a suitable metal precursor and an azolium salt as ligand precursor in the presence of a base. Pioneering work in this field was achieved by the group of Nolan.[194] Further important contributions were made by Organ and co-workers who reported the family of very efficient PEPPSI-based compounds (**p**yridine-**e**nhanced **p**recatalyst **p**reparation, **s**tabilization, and **i**nitiation), one example (**I-144**) of which is shown in Scheme 32.[195] In this case, dissociation of the stabilizing chloropyridine moiety during the *in situ* reduction of the metal center to Pd[0] delivers an NHC-stabilized species, that is highly active in a variety of coupling processes, for example Negishi,[196] Suzuki,[197] Buchwald-Hartwig,[198] and Kumada reactions.[199]

The straightforward modifiability of NHC ligands is also another key factor for their great applicability as steering ligands in inhomogeneous or two-phase catalysis. Combined with the facile tuning of electronic and steric features of the system, this property led to the development of catalysts active and stable in aqueous solution,[200] or immobilized on solid supports.[201] Water as solvent of choice has many benefits, such as its ready availability, environmental friendliness, and safe handling. Thus, different methods were evaluated to modify the generally hydrophobic complexes in order to render them soluble (and stable) in aqueous solutions.[200] The most straightforward approach is the functionalization of the carbene ligand's wingtips with highly hydrophilic substituents, such as ionic or very polar groups. Suitable moieties are amongst others carbonate,[202] sulfonate,[203] ammonium,[73,204] hydroxyl substituents,[205] or protonated functionalities (**I-145**, **I-146**, Figure 21).[206] A different strategy relies on the utilization of ligand motifs deduced from natural products, such as sugar[207] or caffeine derivatives,[208] that usually show a high intrinsic hydrophilicity (**I-147**, Figure 22).
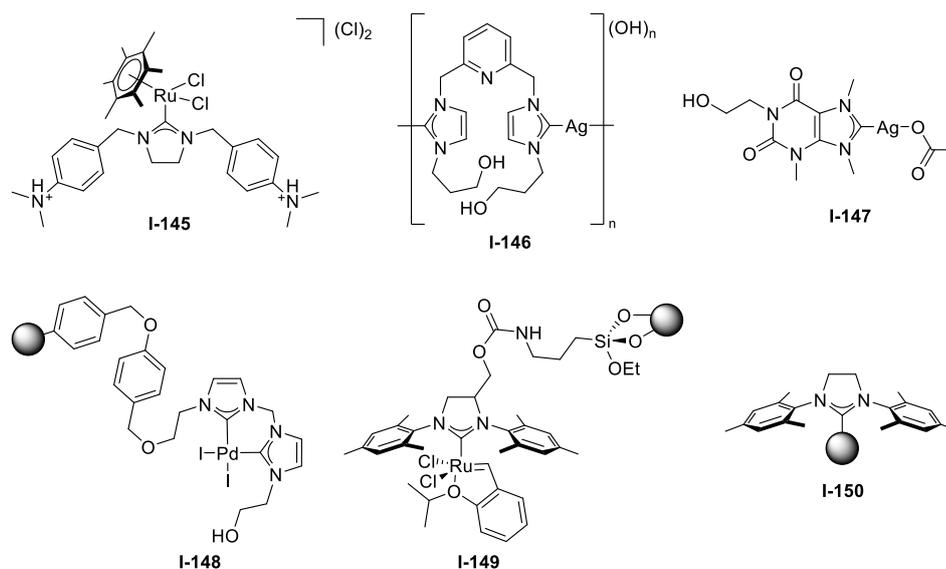

Figure 22.   Top: Examples of water-soluble NHC complexes **I-145**-**I-147** comprising different solubilization methods.[73,205a,208b] Bottom: Examples (**I-148**-**I-150**) for different immobilization strategies for NHC complexes. The black spheres symbolize the solid support material.[209]

A related, but rarely encountered technique is the fixation of NHC complexes on water soluble polymers.[210] The advantage of most of these complexes in catalysis is the facile separation of the products, as they can be extracted from the aqueous reaction mixtures with less polar solvents. The catalytic performance of the hydrophilic catalysts was shown to be comparable to established systems suggesting that water is equally eligible as solvent.[200]

A further way to improve the main drawback of homogeneous catalysts, namely their separation from the product(s), is the immobilization of molecular catalysts on solid supports while maintaining their catalytic capabilities.[201b,211] Compounds featuring *N*-heterocyclic carbenes are valid candidates for this approach, as they can be modified in straightforward manner to serve as anchors for the catalysts *via* attachment of functionalized tethers to them in various ways.[201b] Most reports in this field deal with the modification of the *N*-wingtips, which is to date the easiest synthetic access to immobilized complexes (**I-148**, Figure 22).[209a,212] Alternatively, the ligand's backbone can be synthetically altered leaving both wingtips available for fine-tuning (**I-149**, Figure 22).[209b,213] A third possibility of fixing coordination compounds on supports is *via* metal binding to the surface (**I-150**, Figure 22), however, this is generally not an option for molecular catalysts, as their reactivity is largely reduced. In turn, it is often used for the preparation of NHC-stabilized metal nanoparticles.[209c] The heterogenization can be achieved by a variety of techniques, such as solid phase synthesis,[214] covalent grafting,[209a,213b,215] self-supporting methods,[216] or non-covalent interactions,[217] largely depending on the purpose the assembly is designed for.

Moreover, the development of *N*-heterocyclic carbenes in asymmetric catalysis moves increasingly into the focus of current research efforts.[218] This approach is hampered as most NHCs exhibit freely rotatable wingtips around the C–N bonds and likewise the metal carbene bond is not locked because of its predominant single bond character. To overcome this inherent disadvantages synthetic modification must be implemented in order to restrict or nullify the effect caused by these rotations that would otherwise lead to a partial or complete loss of chiral information. Successful approaches comprise the use of C_2-symmetric ligands with an inhibited rotation of the nitrogen substituents, either by tethering or by steric repulsion by the backbone substituents, such as in **I-151**, **I-152**, and **I-153** (Figure 23). Another possible variation for monodentate ligands is the employment of different ring sizes. Four-, five-, and six-membered *N*-heterocycles feature a nearly planar structure, whereas seven-membered rings deviate significantly therefrom. In case sterically demanding wingtips are bound at the *N*-atoms of the heterocycle, a flipping of the ring is impeded and thus, the system shows persistent chirality, such as **I-154** (Figure 23).[9e]
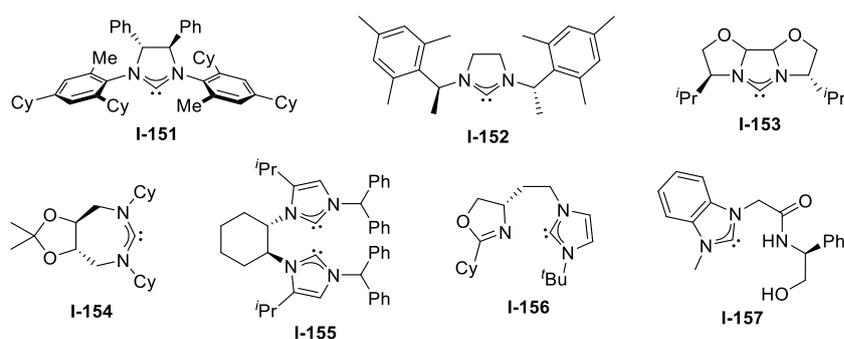

Figure 23. Selected examples of chiral NHC ligands employed as steering ligands for asymmetric catalysis.[9e,219]

Alternatively, multidentate NHC ligands capable of chelating the metal center and conserve the chiral information, such as **I-155, I-156**, or **I-157** (Figure 23), are a viable solution. The majority of the known asymmetric NHC complexes have been reported as stereoselective catalysts in the area of homogeneous hydrogenation. Highly efficient iridium olefin hydrogenation catalysts featuring chelating NHCs have been developed by the groups of Burgess[220] and Pfaltz,[221] whereas Glorius *et al.* synthesized a ruthenium complex based on two chiral, monodentate ligands with an excellent performance in asymmetric hydrogenation reactions.[222]

Yet another field of high versatility and future potential, where *N*-heterocyclic carbenes increasingly gain on importance is the application of coordination compounds for medicinal purposes. For that, especially platinum(II), silver(I) and gold(I) complexes have emerged as suitable targets for metallopharmaceuticals. To date, $(NHC)_2$-type complexes like **I-158** (Figure 24), or compounds with bio-inspired NHC ligands based on as saccharin, cysteine, or caffeine scaffolds (**I-159**, Figure 24) show very promising results as antibacterial and anticancer agents.[223] A significant number of silver(I) NHC entities exhibit extraordinary low minimum inhibitory concentration values against various Gram-positive and -negative bacteria ($< 10\ \mu g\ mL^{-1}$). Compared to the standard reference $AgNO_3$, the NHC-based substances are usually longer therapeutically active, most likely due to a slower liberation of active silver(I) ions. The respective gold(I) complexes are potential anticancer drugs with the focus on mitochondria targeting. The advantage of NHCs for this application is the possibility to adjust the lipophilicity of the complex which is a crucial prerequisite for anticancer activity, as it is heavily depending on the penetration through the mitochondrial membrane.[223] The mechanism of action of the gold-based drugs is assumed to rely on their tendency to selectively bind and thus inhibit the selenoenzyme thioredoxin reductase, which is often overexpressed in human cancer cells.[224]
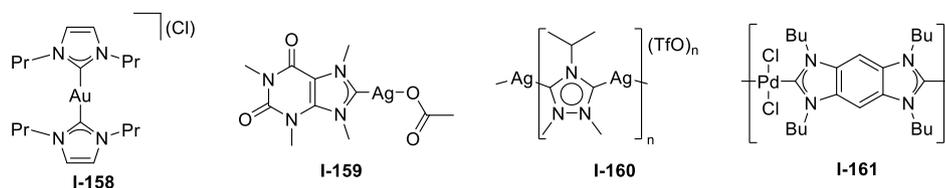

Figure 24. Selected NHC complexes for medicinal applications and organometallic materials: $(NHC)_2$-type Au[I] complex **I-158**, caffeine-based Ag[I] complex **I-159**, as well as Ag[I]- and Pd[II]-based organometallic polymers **I-160** and **I-161**, respectively.

The immense thermal stability of some NHC complexes as well as their steric and electronic tunability renders this compound class also eligible for organometallic materials.[10] Exemplarily, NHC ligands have been modified in order to serve as in linker molecules for metal-organic frameworks (MOFs) resulting in organometallic complexes within the MOF's pores.[225] NHC complexes with long, lipophilic alkyl-wingtips tend to self-assemble and thereby form very air- and moisture-stable liquid crystalline materials stable beyond their clearing point.[226] Including transition metal complexes with tailored *N*-heterocyclic carbene ligands into the side or main chain of organometallic polymers, as in **I-160** and **I-161** (Figure 24), which leads to very interesting properties, such as thermal stability, high conductivity and dynamic behavior.[227] Additionally, these materials show self-healing properties due to the inherent reversibility of metal ligand binding.

Thus, such substances are potential electrical conductors with conjugated di(carbene) linkers allowing electronic coupling between the two coordinated metal centers.

Apart from the applications described in this chapter, *N*-heterocyclic carbene complexes found their way into a plethora of further fields of research, such as metal surface coordination,[209c,228] stabilization of highly reactive intermediates,[229] or the synthesis and tuning of highly luminescent emitters.[230] However, their full account would certainly go beyond the scope of this comprehensive introduction.

2.8   Conclusion

"N-heterocyclic carbenes – the measure of all rings"[9d] – this is the title of a review article by Glorius *et al.* and certainly reflects the importance that NHCs gained over the last 25 years. The preceding chapter in this thesis gave a comprehensive, but by no means complete summary of the cornerstones that render this ligand class so unique. The most frequently applied synthetic procedures for ligand precursors with different substitution patterns were explained and based on that a number of different approaches for the synthesis of NHC metal complexes was presented highlighting the huge variability these ligands introduce to coordination chemistry. Likewise, the electronic properties of *N*-heterocyclic carbenes were described in detail focusing on techniques to assess them experimentally and the factors that predominantly influence them. Another crucial characteristic of this ligand class discussed above is their tunable steric demand. Prominent methods were discussed to elucidate by what means this feature can be quantified and compared. Based on these sections covering NHCs in general, the two following sections intended to introduce the more specific topics of macrocyclic, as well as pyrazole-bridged scaffolds, as these two compound classes are the very basis of this thesis. The last part of this introduction was dedicated to describing the most important applications of *N*-heterocyclic carbenes in a plethora of commercial and scientific areas highlighting their omnipresent importance in modern chemistry.

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3 OBJECTIVE

Ligand scaffolds containing both pyrazole and imidazole heterocycles have been shown to form highly stable complexes with late transition metals ions. The fact that *N*-heterocyclic carbenes are very strong σ-donors is beneficial for a plethora of catalytic applications. Additionally, the pyrazolate entity generally adopts a bridging position by coordinating two separate metal ions and thus allows for an electronic communication between both *via* its π-system. The implementation of these functionalities within a macrocyclic architecture should further increase the stability of the complexes and enable a tuning of the metal centers' coordination geometry by varying the length and nature of the linkers between the heterocycles. Therefore, the initial aim of this work was to design a novel type of pyrazole/imidazole-based hybrid cyclophanes. For this purpose a high yielding and selective macrocyclization protocol needed to be designed.
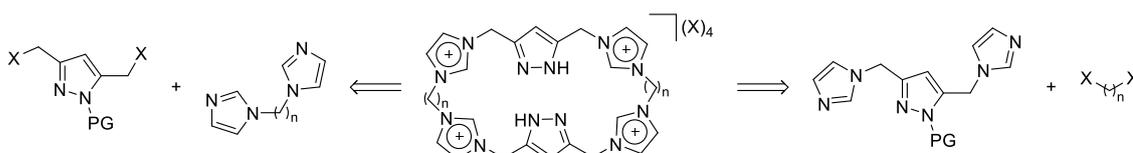
Scheme 33. Retrosynthetic analysis of the desired pyrazole/imidazole-based hybrid architecture.

With the ligand precursor in hand the synthesis of the respective dinuclear nickel NHC complex was envisioned. Subsequently, the effect of different chain lengths of the bridging alkyl moieties was investigated in order to fine-tune the curvature of the complexes' overall structure in order to generate cavities suitable for anion recognition purposes. Additionally, complexation reactions with substoichiometric amounts of metal precursors were studied to evaluate the feasibility of mixed imidazolylidene/imidazolium complexes as starting materials for multinuclear heterometallic NHC compounds.
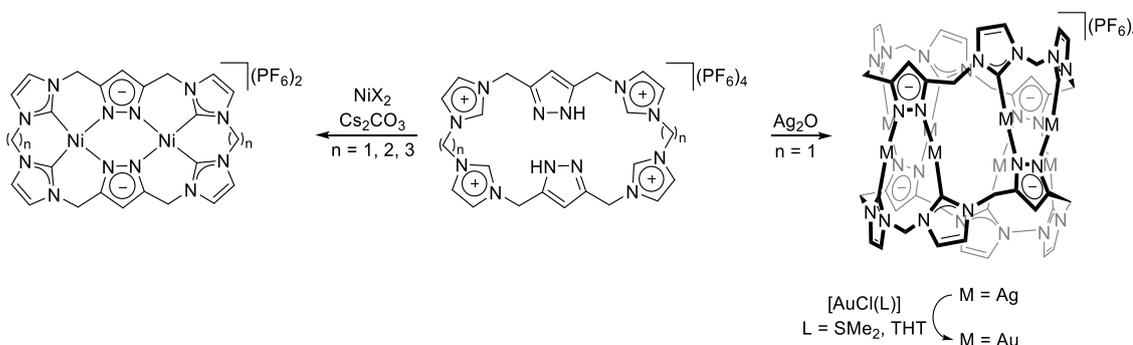
Scheme 34. Envisioned coordination modes of the macrocyclic calix[4]imidazolium[2]pyrazole ligand precursor upon deprotonation and metal coordination.

Furthermore, the synthesis of the respective coinage metal complexes was examined, as the structural prerequisites of Ag^I and Au^I were expected to cause M$_8$L$_2$-type architectures comprising defined cavities that should theoretically be suited for the uptake of guest molecules. In the light of recent advancements in the field of supramolecular chemistry and molecular machines these complexes were then to be tested as organometallic building blocks implemented in sophisticated mechanically interlocked assemblies.

Likewise, the synthesis and comparison of complexes containing related macrocyclic, as well as open-chain tetra(NHC) ligands that exclusively feature carbene donor sites was examined for their structural and reactivity properties.

4 RESULTS –
PUBLICATION SUMMARIES

4.1 Introducing a Pyrazole/Imidazole Based Hybrid Cyclophane: A Hydrogen Bond Sensor and Binucleating Ligand Precursor

Philipp J. Altmann, Christian Jandl, Alexander Pöthig

In this work a novel cyclophane based on methylene-bridged imidazolium and pyrazole units was introduced as a new example of a macrocyclic proligand,[1] that are known for their unique capabilities in anion recognition[2] and metal complexation.[1a,3] The calix[4]imidazolium[2]pyrazole was designed to combine the beneficial features of imidazole moieties on the one hand and the capability of pyrazoles to act as bridging ligand between two metal centers allowing for electronic coupling between them through the ligand.[4] The synthetic approach utilizes the pyrazole-bridged precursor **2**,[5] whose accessibility we were able to improve significantly (Scheme 35). Its treatment with sodium imidazolide afforded bis(imidazole) **3** that subsequently underwent a macrocyclization reaction with methylene bis(triflate),[3b] yielding the imidazolium salt **4-OTf** after deprotection that was further processed to **4-PF₆** *via* anion exchange.
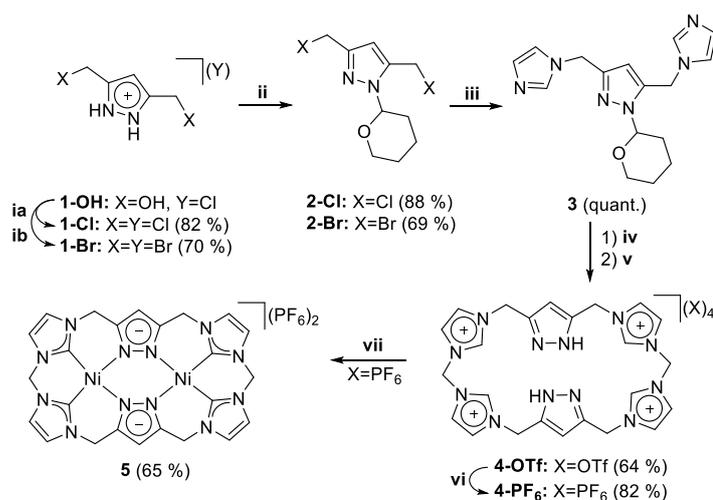
Scheme 35. Synthesis of imidazolium salts **4** and the respective nickel NHC complex **5**: (**ia**) SOCl₂ (neat), 95 °C, 30 min; (**ib**) SOBr₂ (neat), 0 - 40 °C, 2 h; (**ii**) 3,4-dihydro-2*H*-pyran, (DCM), r.t., 16 h; (**iii**) NaIm, (MeCN), r.t., 16 h; (**iv**) CH₂(OTf)₂, (MeCN), -40 °C - r.t., 16 h; (**v**) Tf₂O/H₂O, (EtOH), r.t., 30 min; (**vi**) NH₄PF₆, (H₂O), r.t., 30 min; (**vii**) [NiCl₂(PPh₃)₂], Cs₂CO₃, (MeCN), 70 °C, 16 h.

The substitution of triflate for hexafluorophosphate was shown to have a tremendous effect on the molecular structure of **4** in the solid state. Whereas in **4-OTf** the cation forms almost perfectly unstrained hexagons with alternatingly oriented five-membered rings, in **4-PF₆** the conformation changes drastically producing a bowl-shaped cavity. This instance is caused by the weaker coordinating hexafluorophosphates which cause the cyclophane to tightly bind an acetonitrile solvent molecule instead of interacting with the anions, as was found for **4-OTf**. An extensive Hirshfeld analysis[6] underlined these findings suggesting that in the case of **4-OTf** the H···O contacts to different triflate anions can be assigned as the dominant interaction, whereas for **4-PF₆** a major fraction is directed towards the tightly bound MeCN. Consequently, the acetonitrile

molecule perfectly fits into the cavity, rationalizing why one equivalent of the solvent could not be removed *in vacuo* (Figure 25).
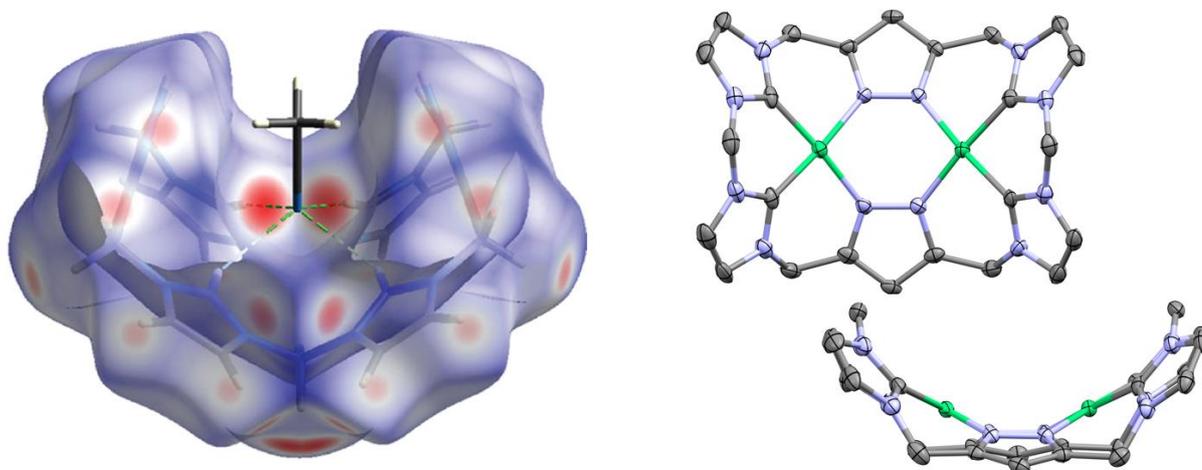
Figure 25. Left: Supramolecular recognition of MeCN by the cation of **4-PF₆** in the solid state shown by Hirshfeld surface analysis.[6] Directed hydrogen bonding (green) from all four imidazolium C2 protons towards a MeCN nitrogen acceptor. Right: Solid state structure of dinuclear complex **5**. View from two perspectives showing the bowl-shaped arrangement of the complex. Ellipsoids are at the 50 % probability level. Hydrogen atoms, counterions and co-crystallized solvent molecules are omitted for clarity.

To further examine the versatility of the cyclophanes the synthesis of the respective dinuclear nickel(II) complex was envisioned. A strategy employing the external base Cs₂CO₃ in combination with [NiCl₂(PPh₃)₂] as metal precursor yielded the desired compound **5** in good yields after workup (Scheme 35). Its ¹H NMR spectrum indicated a very rigid framework, even at elevated temperatures with an overall reduced symmetry in comparison to the precursor **4-PF₆**. The proposed composition of the NHC complex was further evidenced by mass spectrometry and elemental analysis. The molecular structure in the solid state was determined by single crystal XRD and revealed an overall bowl-shaped constitution with two Ni^II centers coordinated in a square planar fashion by two carbon and two nitrogen donors each (Figure 25). The two mean planes established by each Ni ion and its coordinating atoms form opening angles of 122–123° resulting in a wide open cavity that is occupied by hexafluorophosphate ions in the solid state.

The synthetic procedure towards the calix[4]imidazolium[2]pyrazole cyclophane and initial experiments towards its supramolecular and metal binding capabilities can be seen as the fundamentals of a highly divergent chemistry that can be pursued from this point on.

Parts of the results in this publication have already served for examination purposes in: P. J. Altmann, *Master's Thesis*, Technische Universität München, Munich, **2014**.[7]

4.2   Capsoplexes: Encapsulating Complexes *via* Guest Recognition

Philipp J. Altmann, Christian Jandl, Alexander Pöthig

The synthesis of a new dinuclear nickel NHC complex capable of selectively recognizing and self-assembling with guests *via* a tennis-ball fashioned encapsulation is presented. Well-established approaches for anion sensors rely on the design of polydentate ligands which adopt a defined configuration upon metal complexation as is the case for pacman complexes[8] or azacryptand complexes.[9] A fundamentally different strategy involves the synthesis of cationic metallocages that create defined cavities in a different way, namely using a coordination driven self-assembly of polydentate ligands and capped metal nodes.[10] The supramolecular concept presented in this work utilizes the guest-induced formation of a capsule that is stabilized through non-classical hydrogen bonds and Coulomb interactions between the anion and the metal centers. Hence, it combines the advantages of a specially designed ligand system with the ability to create molecular capsules by self-assembly, in which a small guest is incorporated.

Starting from the ethylene-bridged NHC ligand precursor **6-PF$_6$** that was obtained *via* the macrocyclization protocol established earlier for the CH$_2$-bridged congener,[11] the dinuclear Ni^{II} complex **7** was obtained by reaction with anhydrous Ni(OAc)$_2$ under basic conditions (Scheme 36).
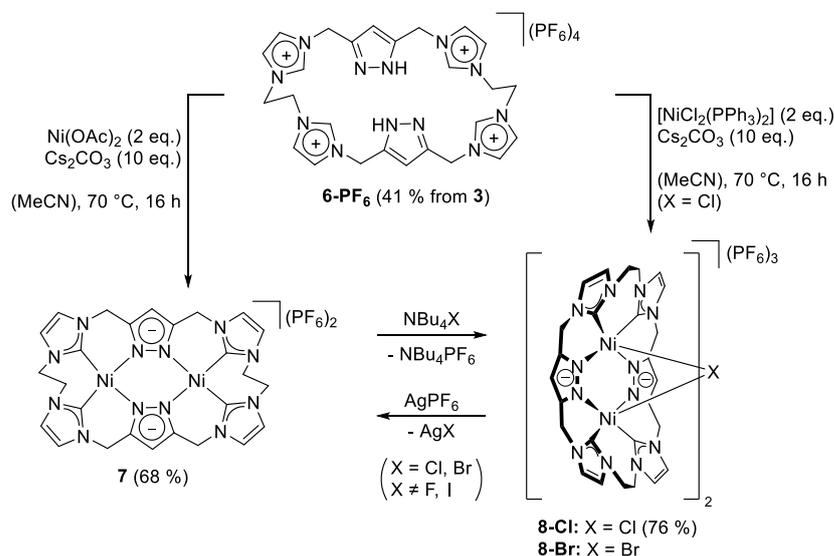
Scheme 36.   Synthesis of dinuclear complex **7** and tetranuclear complex **8** (X = Cl, Br), as well as interconversion of both *via* addition and removal of halides.

The compound adopts a saddle-shaped structure with one hydrogen atom of each ethylene bridge pointing towards the inner cavity of the bowl (H22B, H9B; Figure 27). In that way a cavity is generated that features the ideal prerequisites to host small anions or molecules. Indeed, it was observed that the addition of chloride or bromide anions led to the formation of a new species as followed by NMR spectroscopy, whereas fluoride or iodide did not result in a change. In the ^{1}H NMR spectrum virtually all signals shift to a higher field and some significantly broaden

(Figure 26). The identical spectrum was obtained when performing the reaction between **6-PF$_6$** and [NiCl$_2$(PPh$_3$)$_2$], instead of the acetate precursor. The elemental analysis of the isolated product **8-Cl** proved the composition of two Ni$_2$L^{Et} cations, one chloride, as well as three PF$_6$ anions and DOSY spectroscopy revealed a substantially larger solvodynamic radius as compared to **7**.
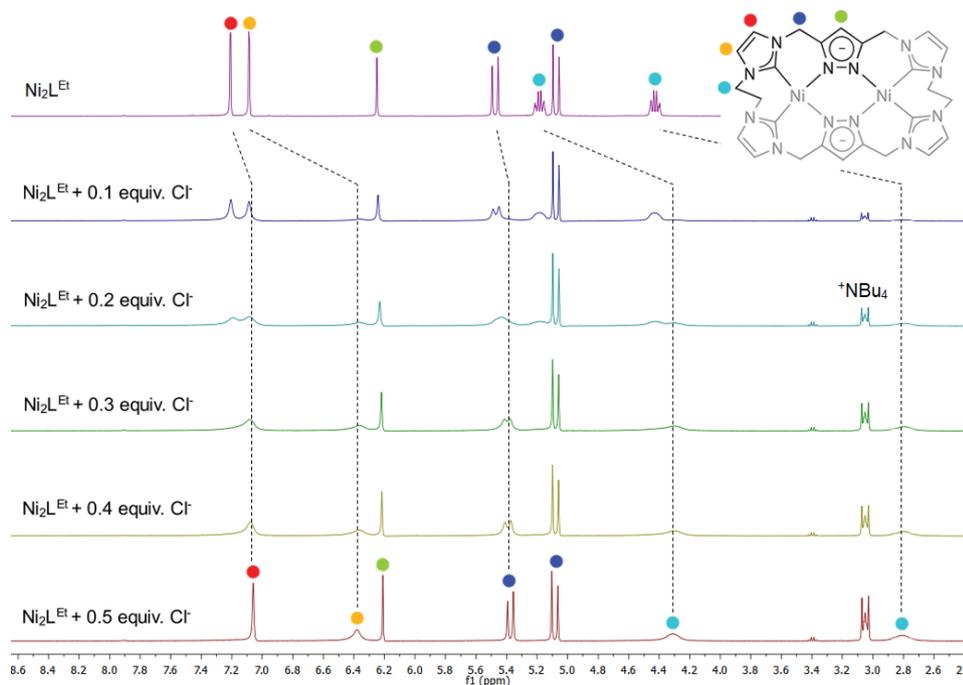
Figure 26.   Titration experiments monitored by ^{1}H NMR spectroscopy showing the signal changes upon stepwise addition of 0.5 equivalents NBu$_4$Cl to Ni$_2$L^{Et}-complex **7** in CD$_3$CN.

The solid state structures of the chloride and bromide "capsoplexes" **8-Cl** and **8-Br** were determined *via* single crystal XRD. In both cases, the halide is encapsulated in a tennis-ball-like fashion by two symmetry-equivalent cationic complex fragments (Figure 27). The nickel centers form a distorted tetrahedron around the anion, exhibiting Ni–X distances that are significantly higher than the sum of their ionic radii,[12] indicating an exclusive Coulomb attraction between metals and halides. Additionally, one hydrogen atom of each of the four involved ethylene groups is pointing towards the central cavity, thus stabilizing the capsule *via* H-bonding to the anion. These results render these compounds highly promising for small molecule activation *via* substrate recognition, encapsulation, catalytic transformation, and subsequent release of the product.
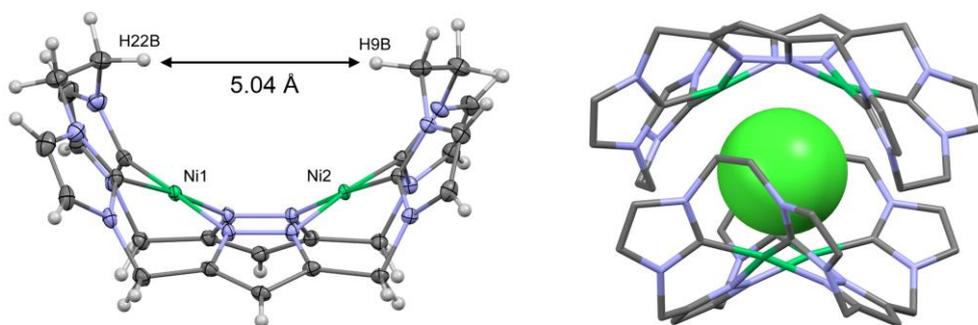
Figure 27.   Left: ORTEP representation of **7** at the 50 % probability level (counter ions, solvent molecules and disorders have been omitted for clarity). Right: Molecular structure of capsoplex **8-Cl** (non-encapsulated counter anions and solvent molecules have been omitted for clarity). The dinuclear complexes are shown as capped sticks, the encapsulated anions in the space filling model.

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4.3 A hybrid Imidazolylidene/Imidazolium Nickel NHC Complex – An isolated Intermediate

Philipp J. Altmann, Michael Ehrenreich, Alexander Pöthig

Multidentate ligand systems featuring numerous (different) donor sites and a macrocyclic framework are powerful metal-binding scaffolds and tend to yield unexpected and potentially exciting complexes.[1a] This is especially true for the compound reported in this work. The trinuclear nickel(II) NHC complex is a rare example of a coordination compound containing imidazolium next to imidazolylidene moieties. Therefore, it can be understood as a trapped reaction intermediate that occurs during the synthesis of the respective [Ni$_2$L](PF$_6$)$_2$-type product **5**.[11]

During the studies towards the synthesis of partially occupied and mixed-metal NHC complexes, the macrocyclic imidazolium salt **4-PF$_6$** was reacted with differing amounts and types of Ni^{II} precursors and external bases of different strength, such as carbonates, hydrides, or silylamides. For certain stoichiometries, especially those with low amounts of Ni^{II} precursor and strong bases, for example KN[Si(CH$_3$)$_3$]$_2$, a novel compound could be detected in the crude product mixture, namely the [Ni$_3$L$_2$Cl$_2$](PF$_6$)$_4$-type complex **9** (Scheme 37).
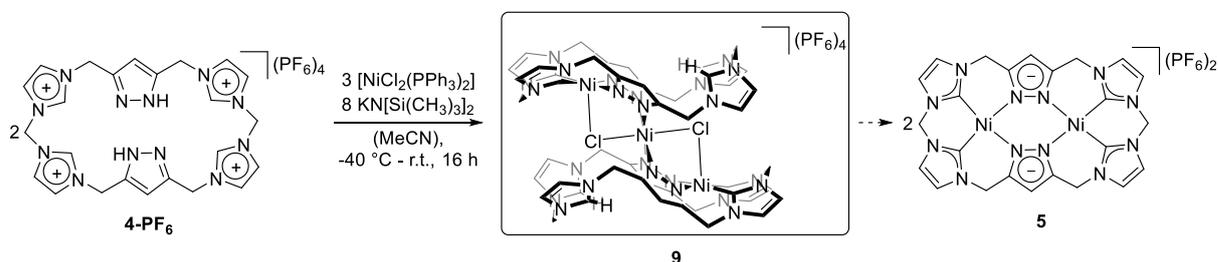
Scheme 37. Formation of the hybrid imidazolium/imidazolylidene complex **9**, an isolated intermediate occurring during the reaction from **4-PF$_6$** to **5**. As a simplification it is assumed that KN[Si(CH$_3$)$_3$]$_2$ is the only base present, although its conjugate base HN[Si(CH$_3$)$_3$]$_2$ could also be involved.

The cationic [Ni$_3$L$_2$Cl$_2$]$^{4+}$ fragment of **9** comprises two partially deprotonated imidazole/pyrazole hybrid ligand molecules, three Ni^{II} ions and two μ^2-bridging chloride anions (Figure 28). The involved nickel ions exhibit fundamentally different coordination geometries and donor sites. The Ni^{II} center in the complex's heart is ligated by four nitrogen atoms – one from each pyrazole in the complex – in its equatorial plane and two capping chlorides in *trans*-position with respect to each other, resulting in an overall octahedral geometry (Figure 28, left). The two remaining nickel(II) cations are coordinated by *N*-donors of the two proximal pyrazolate moieties, two carbene carbon atoms generated by C–H deprotonation of the former imidazolium rings and one capping chloride anion, resulting in a square-pyramidal coordination pattern. The distance between the neighboring nickel ions (3.4521(5) Å) is significantly above the sum of the van der Waals radii of 3.26 Å,[13] thus, metallophilic interactions can be ruled out as structure-determining factor.

The octahedral and square-pyramidal coordination of the metal centers in **9** is differs significantly from the square-planar motif that is found for **5**,[11] which **9** is converted to upon further deprotonation of the imidazolium heterocycles in the presence of additional Ni[II] ions. Hence it becomes clear that the macrocyclic ligand is able to stabilize three distinctly different coordination numbers and geometries which certainly shows its high versatility. Additionally, one can reason that the involved nickel(II) ions transient from an octahedral to a square-planar coordination environment *via* a square-pyramidal intermediate stage during the course of the reaction from **4-PF₆** to **5**.[11] Another striking difference from established coordination compounds featuring this ligand is its overall chair-like conformation, which is in clear contrast to the bowl-shape in **5**,[11] and the flat arrangement with all donor atoms facing in one direction, as was found for complexes of the type $[M_8L_2]^{4+}$ (M = Ag and Au).[14] As expected, the non-coordinating azolium entities in **9** are protonated at the NCN carbon atoms. This could crystallographically be proven by the overall charge balance in the molecular structure, the distinct interaction of these positions to a proximal, co-crystallized acetonitrile molecule (Figure 28, right), and the fact that both hydrogen atoms could be located in the difference Fourier maps allowing for their free refinement.
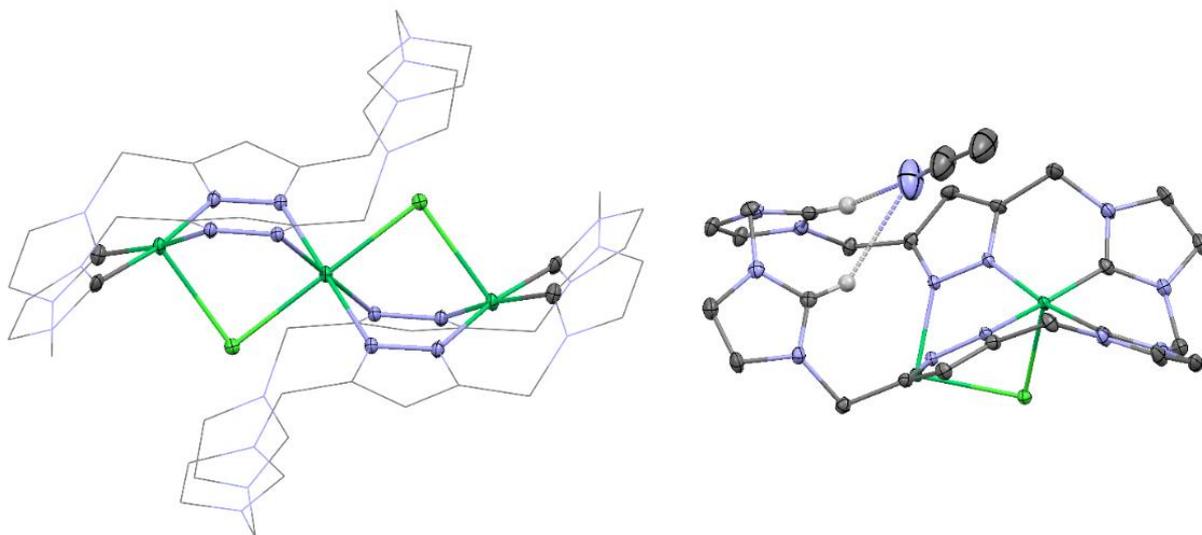
Figure 28.   Left: First coordination sphere of the Ni[II] ions in **9**. Right: Molecular structure of the asymmetric unit of **9** and one co-crystallized molecule of acetonitrile. The interactions between the imidazolium-bound hydrogen atoms and the nitrogen atom of the adjacent acetonitrile molecule are illustrated by dashed lines. Remaining hydrogen atoms, solvent molecules and hexafluorophosphate counterions have been omitted for clarity in both cases.

The two hexafluorophosphate anions in the asymmetric unit are located at positions where they are able to form several favorable hydrogen bonds throughout the packing. Thus, they are crystallographically well-behaved in a way that they are not disordered, which is uncommon, as oftentimes heavy disordering of these weakly coordinating, spherical anions is encountered. Overall, the molecular structure of **9** in the solid state presented in this manuscript allows for a valuable insight into the formation mechanism of coordination compounds involving complex, multidentate ligand motifs. Potentially, this compound could serve as precursor to mixed-metal NHC complexes or as CO_2-reducing electrocatalyst.

4.4 Pillarplexes: A Metal-Organic Class of Supramolecular Hosts

Philipp J. Altmann, Alexander Pöthig

Supramolecular chemistry has historically grown to be a field largely dominated by organic chemistry.[15] Amongst the most prominent substances for this purpose are pillar[*n*]arenes, cucurbit[*n*]uriles and cyclodextrines.[16] As most of these well-established systems lack proper postsynthetic modifiability,[17] metal functionalities came slowly into the focus as novel building blocks with a variety of beneficial properties.[18] On the other hand, metal complexes often exhibit unfavorable features that limit their applicability for these purposes drastically.[19] We were able to overcome these challenges with the introduction of octanuclear noble metal complexes featuring the imidazole/pyrazole hybrid ligand reported earlier (Scheme 38).[11]
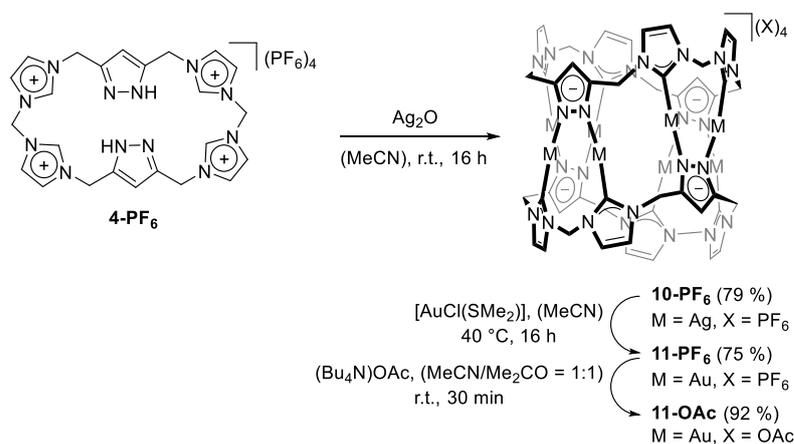
Scheme 38. Synthesis of **10-PF$_6$**, transmetalation with [AuCl(SMe$_2$)], and subsequent anion exchange with (Bu$_4$N)OAc to afford **11-PF$_6$** and **11-OAc**, respectively.

The NHC complexes of the type [M$_8$L$_2$]X$_4$ (M = Ag, Au; X = PF$_6$, OAc) feature a tubular cavity of perfect size to host small or linear molecules. Titration experiments with 1,8-diaminooctane as model guest substrate revealed strong highfield shifts of the CH$_2$-protons of the amine's alkyl chain in dependence on the amount of host present in solution (Figure 29). The dissociation constants calculated for this process *via* line fitting of the guest's NMR resonances are comparable to that observed for the analogous guest with a functionalized pillar[5]arene in a 1:1 mixture of MeCN/H$_2$O.[17a] The host-guest assembly (M = Au; X = PF$_6$) could be crystallized and studied by single crystal XRD confirming the uptake of the diamine by the host complex (Figure 29). The molecular structure of **11-PF$_6$** consists of eight gold atoms situated between two of the pyrazolato/imidazolylidene hybrid ligands in a way that the metal ions are bound to one nitrogen and one carbon donor each. This leads to a staggered arrangement of the two ligand molecules by 90° relative to each other. The structural prerequisite of the ligand leads to several aurophilic Au–Au contacts between 2.987(1) and 3.005(1) Å, that are all well below the sum of the van der Waals radii of 3.80 Å.[20] The pillarplex's cavity dimensions of 11.7 · 4.3 Å suggest a high selectivity for linear over branched substrates. Accordingly, we proved by size exclusion

experiments that the Au$_8$-based host is indeed size selective for linear over six-membered aromatic molecules. This property is unprecedented, as all of the organic host-compounds include either both (pillar[n]arenes, cucurbit[n]urils ($n \geq 6$) and cyclodextrins) or neither of both (cucurbit[5]uril).
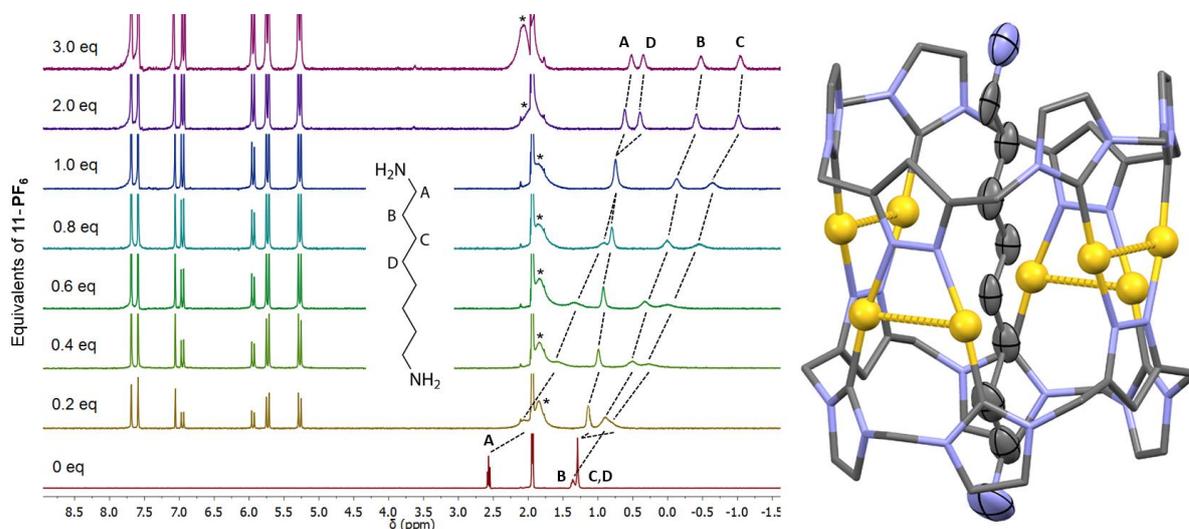
Figure 29.   Left: ^{1}H NMR titration of **11-PF$_6$** in CD$_3$CN into a solution of 1,8-diaminooctane in CD$_3$CN. The asterisk marks the water signal. The signals between 5 and 8 ppm are assigned to **11-PF$_6$**. Electronic shielding by the cavity of **11-PF$_6$** (host) leads to a highfield shift of the protons (**A−D**) of 1,8-diaminooctane (guest). A K_d value of 24.0 $\pm$ 5.4 µM was calculated. Right: Solid-state molecular structure of the cation of **11-PF$_6$** shown in capped sticks (gold(I) centers as balls) with 1,8-diaminooctane co-crystallized within the cavity. Ellipsoids are shown at 50 % probability. Hydrogen atoms, counterions, and solvent molecules are omitted for clarity.

Another enormous advantage of the pillarplexes is their salt-like nature which enables an easily tunable solubility *via* simple anion exchange reactions. The complex with hexafluorophosphate anions is soluble in polar solvents, whereas the acetate congener dissolves readily in water ($\approx$ 1 g mL^{-1}). Moreover, the Au$_8$ complexes exhibit strong emission in the blue region of the visible spectrum upon UV-excitation due to the aurophilic contacts in the structure. This property can be utilized for a quantitative determination of the binding constants given the substrate is a luminescence-quencher.[17a] Consequently, the emission signal of **11-OAc** declines depending on the amount of 1,8-diaminooctane present in solution with enough significance to perform a quantitative analysis. A dissociation constant of 11.9 $\pm$ 1.9 µM was determined in aqueous solution which is approximately half of the value found for **11-PF$_6$** in MeCN, most likely due to the different solvent polarities. To verify the quenching results, host-guest titrations followed by ITC analysis were conducted, resulting in a K_d of 7.5 $\pm$ 0.4 µM which is in good accordance.

In conclusion, pillarplexes are an exciting, novel class of organometallic host-compounds with a high selectivity for linear molecules. Additionally, the solubility of these metallocavitand complexes is easily tunable by simple anion exchange reactions so that these compounds can in principal be applied for supramolecular recognition in a manifold of solvents. The Au$_8$ congener with acetate counterions is emissive in aqueous solutions enabling the determination of dissociation constants *via* a straightforward luminescence quenching approach that were confirmed by ITC experiments. Based on the results a widespread spectrum of further modifications and applications of these tremendously versatile and stable metallocavitands is expected.

4.5   A pH-Dependent, Mechanically Interlocked Switch: Organometallic [2]Rotaxane vs. Organic [3]Rotaxane

Philipp J. Altmann, Alexander Pöthig

In this work the first [2]rotaxane featuring a functional organometallic host is presented. It resembles a rare example of a mechanically interlocked assembly with a metal-organic ring component as structural element.[21] These systems are especially appealing because metal ions potentially introduce novel functions, such as catalytic and sensing properties, or as structural components in metallo-supramolecular assemblies,[22] into this research field which is historically dominated by exclusively organic systems. This is of particular interest, as rotaxanes are crucial building units for a variety of molecular switches,[23] ratchets,[24] shuttles,[25] or other elaborated nano-devices.[26]

Upon double capping of 1,12-diaminododecane hosted in the pillarplex **10-OTf** *via* reaction with 3,5-di-*tert*-butylbenzoic anhydride in the presence of *N,N*-diisopropylethylamine (DIPEA) the [2]rotaxane **12** is obtained in nearly quantitative yield (Scheme 39). The high yield for this reaction is certainly uncommon and can be explained by the very tight guest-binding of **10-OTf** in dimethylformamide.[14] Consequently, only traces (< 1 %) of unstoppered pillarplex entity were detected in the crude product for the conditions applied.
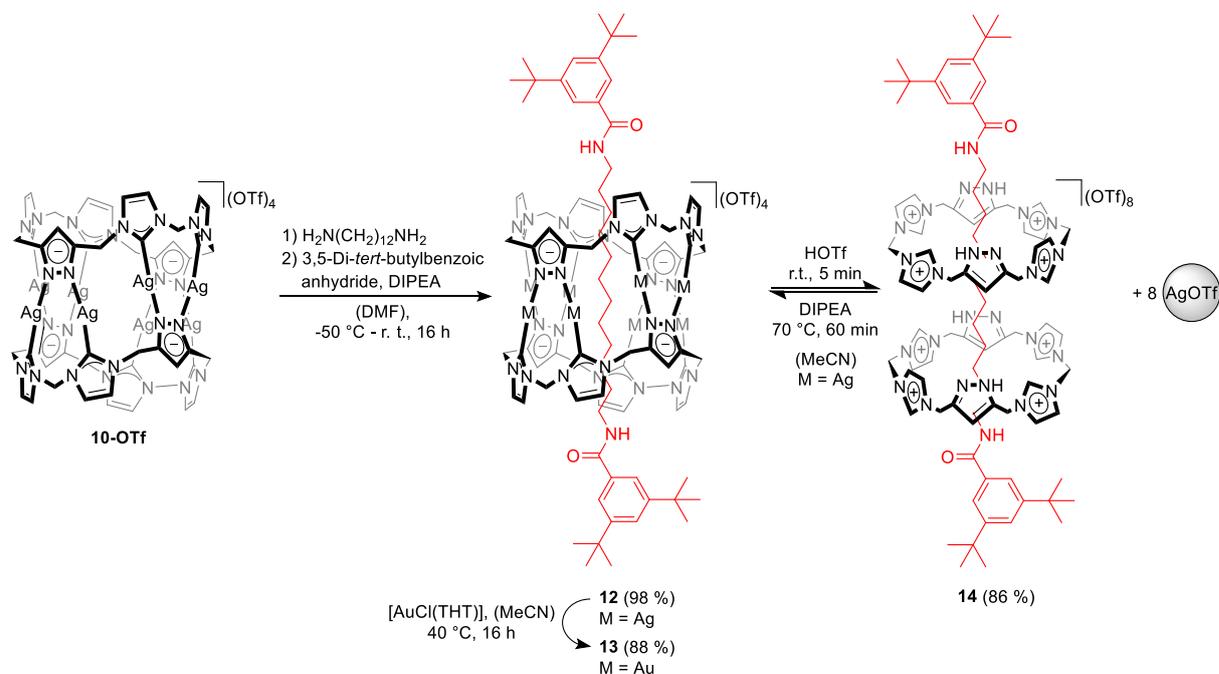
Scheme 39.   Synthesis of Ag₈-based [2]rotaxane **12**, reversible acid/base-assisted interconversion of **12** and the organic [3]rotaxane **14**, as well as transmetalation to the isostructural Au₈ compound **13**.

The rotaxane formation was confirmed by NMR spectroscopy, mass spectrometry, elemental analysis, as well as single XRD. The molecular structure in the solid state proves vividly that the alkyl chain is hosted within the host's cavity and the newly formed, bulky benzamide stoppers prevent its dethreading (Figure 31, top). The pillarplex framework fully retains its structural integrity and features four argentophilic contacts with Ag–Ag distances between 3.1049(7) and 3.1442(7) Å, analogous to the Au$_8$ congener.[14] To confirm that its reactivity remains unaltered, rotaxane **12** was reacted with 8 equivalents of [AuCl(tht)]. The transmetalation proceeded indeed smoothly and yielded the Au$_8$ rotaxane **13** in excellent yields. Although the assembly contains luminescence quenching amide functional groups, **13** is emissive in the solid state (λ_{ex} = 335 nm, $\lambda_{em,max}$ = 425 nm) with a quantum yield of Φ = 23 %.

Key feature of the organometallic rotaxane is its acid-assisted transformation to an exclusively organic [3]rotaxane *via* de-coordination of the involved metal centers and re-protonation of the ligand's binding sites. During optimization of the conditions for this reaction it became obvious that the interlocked nature of **12** protects the organometallic host complex from protic degradation to a certain extent. The free pillarplex **10-OTf** decomposes to the protonated **H$_6$L(X)$_4$** (X = OTf, CF$_3$COO) scaffolds in the presence of excess trifluoroacetic acid instantly whereas the corresponding [2]rotaxane **12** decays over the course of approximately one day with a half-life of $T_{1/2} \approx$ 3 h under analogous conditions. The sterical prerequisite of the rotaxane assembly retains the two cyclophanes in spacial proximity slowing down the complex's decomposition by a factor > 1000. This property is well-known for catenanes, but the observation of a stabilizing "rotaxand-effect" as observed for **12**, is unprecedented.[27]

When treating the [2]rotaxane **12** with an excess of triflic acid, a rapid reaction to the [3]rotaxane **14** without cleavage of the amide groups occurred. Its formation was confirmed by ^{1}H NMR spectroscopy which contains a newly formed signal at approximately 9.5 ppm caused by the protons at the C2-imidazolium position originating from HOTf (Figure 30).
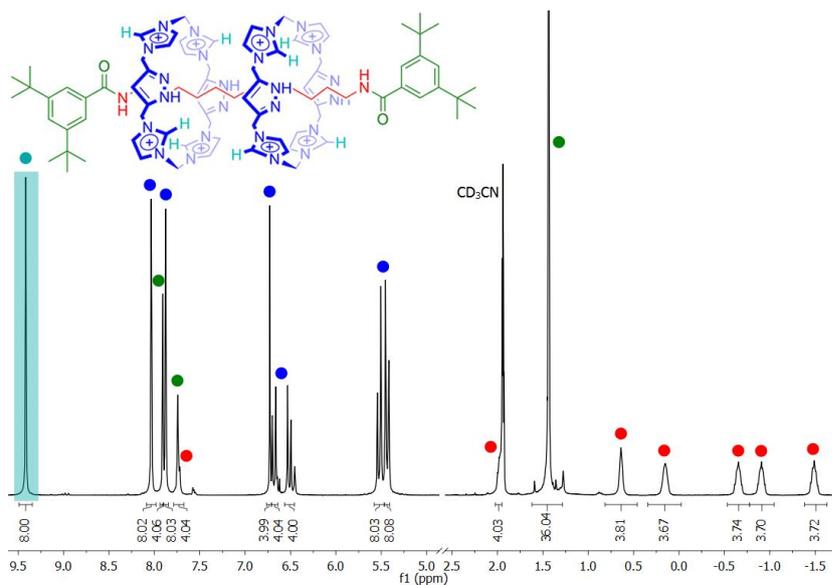
Figure 30.   ^{1}H NMR spectrum of **14** in CD$_3$CN (blank area between 2.5 and 5 ppm is left out intentionally for clarity). The colored dots in the spectrum correspond to the color code applied to **14** shown above. The characteristic signal at 9.5 ppm assignable to the protons bound to the C2-imidazolium carbon atoms is highlighted in turquoise.

No dethreading of the H_6L macrocycles was observed even at elevated temperatures. The solid-state structure inevitably proves the metal-free [3]rotaxane (Figure 31). The two cyclophanes in **14** adapt positions along the alkyl axle that are approximately 2.5 Å further apart from each other as compared to their distance in **12**, most likely due to an increased steric and Coulomb repulsion.
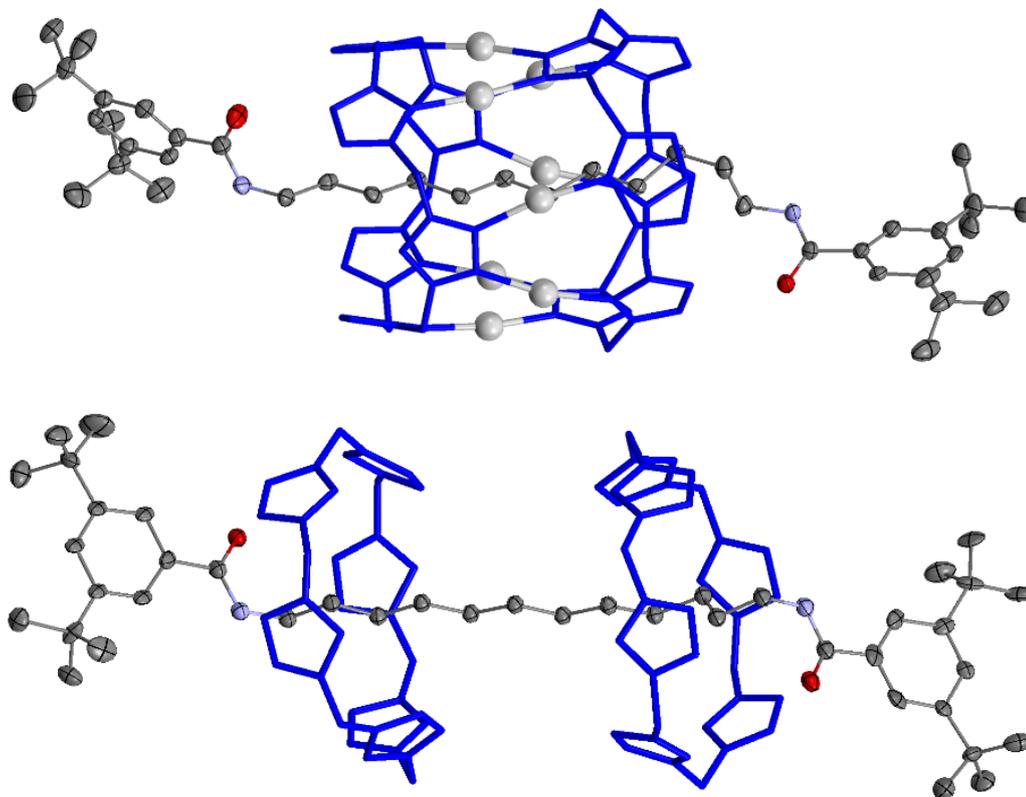
Figure 31.   Solid-state molecular structures of the cations of **12** (top) and **14** (bottom), respectively. The macrocyclic moieties are shown in blue capped sticks (silver(I) ions as silver balls), the axle in ORTEP representation. Ellipsoids are shown at 50 % probability. Hydrogen atoms, counterions, disorders and solvent molecules are omitted for clarity.

Additionally, control experiments showed that no rotaxane is formed in a mixture of proligand **4-OTf** and 1,12-diaminododecane under analogous amidation conditions as applied for the synthesis of **12**. The transformation of **12** to **14** was found to be reversible in a way that addition of a suitable base to a mixture of **14** and the released Ag^I ions at elevated temperature led to the re-formation of **12**. This process can be cycled multiple times without significant loss of material, rendering the rotaxane system a pH-dependent switch. This type of functionality is unprecedented in literature and potentially enables a variety of exciting future applications.

4.6 Exploring Coordination Modes: Late Transition Metal Complexes with a Methylene-bridged Macrocyclic Tetra(NHC) Ligand

Philipp J. Altmann, Daniel T. Weiss, Christian Jandl, Fritz E. Kühn

A fusion of NHC chemistry that has become a key player for homogeneous catalysts,[28] photoluminescent materials,[29] and substances applicable for medicinal purposes,[28d,30] with macrocyclic ligand patterns resulted in highly beneficial frameworks for transition metal coordination.[1a,11,31] Based on the preceding report on an iron complex coordinated by a methylene-bridged tetra(NHC) ligand,[2c,32] this article significantly widens the scope of this powerful, highly symmetrical scaffold. The fundament of this work was the synthesis of the tetranuclear silver(I) compound **16** that was then successfully employed in transmetalation reactions for the synthesis of the respective gold(I), nickel(II), palladium(II) and platinum(II) complexes **17**-**20** (Scheme 40).
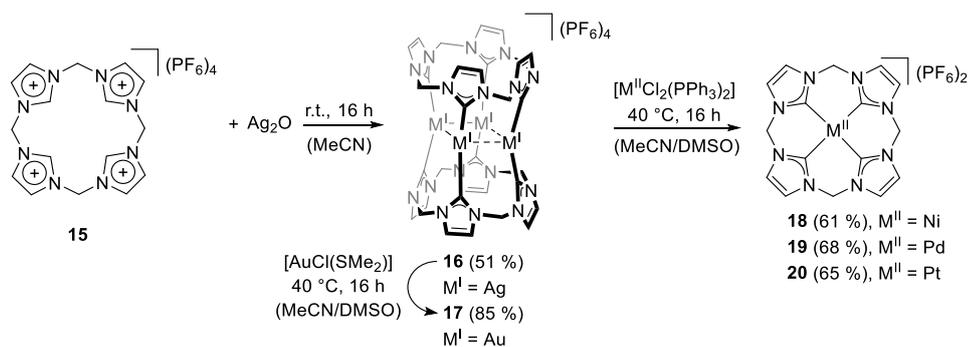
Scheme 40. Synthesis of macrocyclic, tetranuclear silver(I) NHC complex **16** and transmetalation reactions to yield the isostructural gold(I) compound **17**, as well as the mononuclear complexes **18**-**20**.

The highly air and moisture stable silver(I) complex **16** was obtained *via* a straightforward reaction of **15** with silver(I) oxide in acetonitrile at room temperature for 16 h. In consistency with all analytics the complex was found to exhibit a box-type coordination motif with four silver(I) centers sandwiched between two of the macrocyclic ligands (Figure 32). This structural prerequisite leads to close Ag–Ag distances of 3.1747(3) and 3.2365(3) Å, both more than 0.2 Å below the sum of the respective van der Waals radii of 3.44 Å.[33] Therefore, the molecular structure of **16** can be understood as the result of a delicate equilibrium between out-of-plane twisting of the macrocyclic ligand, metallophilic interactions and the quasi-linear coordination of the silver ions. In contrast, a recently reported silver(I) NHC complex based on very similar ligand framework, namely, a cyclophane consisting of four substituted imidazolylidene moieties linked alternatingly by methylene and ethylene bridges forms a structure with two silver(I) ions coordinated in the ligands' cavities and the two remaining ones in bridging positions.[1b] This example shows very elegantly, how putatively minor ligand modifications may lead to drastic changes in terms of their coordination behavior.

Based on these findings it was of our interest to test whether the respective Au(I) complex would be isostructural to **16** and exhibit photoluminescent properties due to aurophilic contacts. Indeed, a straightforward transmetalation approach with [AuCl(SMe$_2$)] yielded the gold complex **17** in good yields. Spectroscopic and structural analysis revealed the identical coordination pattern as found for **16**. The Au–Au distance of 3.1482(5) Å is even shorter compared to the silver complex and consequently far below the sum of the van der Waals radii of 3.80 Å.[20]
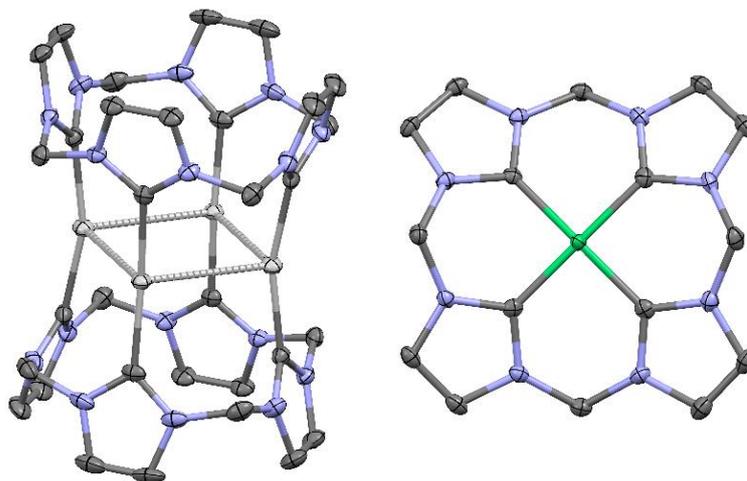
**Figure 32.**   ORTEP style representation of the cationic fragment of **16** (left) and **18** (right) with ellipsoids shown at the 50 % probability level. Hydrogen atoms, co-crystallized solvent molecules, and hexafluorophosphate anions are omitted for clarity.

Photophysical measurements of the tetranuclear Au^I complex **17** revealed a strong photoluminescence in the solid state with a quantum yield of Φ = 31 % (Figure 33). To further elucidate the origin of the photoluminescent properties of **17**, both the mononuclear **[Au(Mono)$_2$]** complex[34] bearing two *N*-methyl-substituted imidazolylidene ligands and the dinuclear **[Au$_2$(Bis)$_2$]** complex[35] with two methylene-bridged, *N*-methylated bis(imidazolylidene) ligands were reproduced and tested for emission properties. Interestingly, the tetranuclear and the mononuclear Au(I) complexes exhibit significant emissions, whereas the dinuclear complex is non-emissive (Figure 33). As the coordination of the gold atoms in all three complexes is very similar, the diverse photoluminescent properties arise from the varying degree of aurophilic interactions that the compounds are capable to form.[20,34-36] In the case of **17** those contacts are of intramolecular, for **[Au(Mono)$_2$]** of intermolecular nature.[34,36a] In contrast, **[Au(Bis)$_2$]** is not able to form either of both due to sterical restrictions and therefore does not show any luminescence.

17: Φ_{em} = 31%
λ_{max} = 442 nm

[Au$_2$(Bis)$_2$]: Φ_{em} = 0

[Au(Mono)$_2$]: Φ_{em} = 56%
λ_{max} = 423 nm
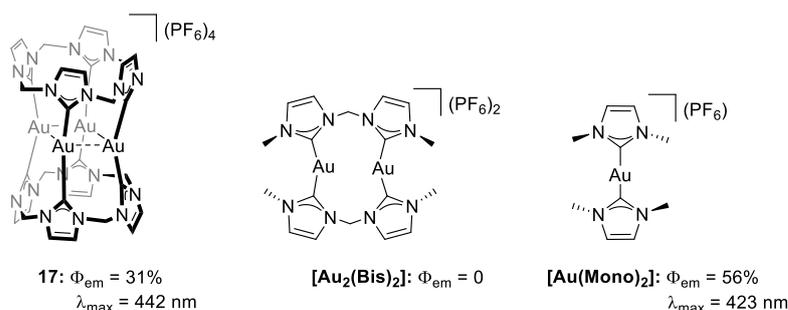
Figure 33.   Gold(I) NHC complexes **17**, **[Au2(Bis)2]**,[35] and **[Au(Mono)2]**[34] with their corresponding quantum yields and emission maxima in the solid state.

To further extend the scope of this ligand motif the group 10 metal complexes were prepared. The transmetalation reaction between **16** and $[M^{II}Cl_2(PPh_3)_2]$ (M^{II} = Ni, Pd, Pt) proceeded readily and the corresponding mononuclear products **18**, **19** and **20** were obtained in good yields after workup (Scheme 40). As expected, the metal ions are coordinated in a nearly square planar fashion with C–M^{II}–C angles close to 180° (Figure 32). With a shrinking size of the central metal ion (Ni < Pd ≈ Pt), the two carbene carbon atoms on opposite sides of the metal center approach each other increasingly, leading to a stronger deformation of the macrocycle to compensate for the decreasing size of the cavity in its center. This trend was confirmed by variable temperature NMR and DFT studies suggesting that only in the case of Ni^{II} the twisting of the macrocyclic ligand can be frozen at temperatures over -100 °C due to the larger deformation of the ligand scaffold (Scheme 41).

$\Delta G^{\ddagger}$ = 9.5 kcal/mol

18-GS1   **18-TS**   **18-GS2**
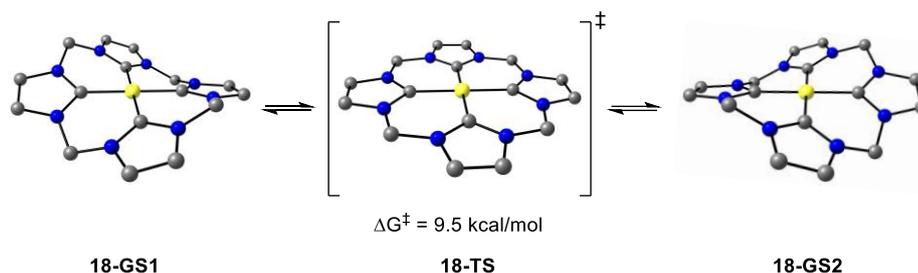
Scheme 41. Calculated ground state and transition state geometries for the ligand vibration of Ni complex **18** that is frozen at -65 °C. (GS: ground state, TS: transition state).

4.7 Structural Diversity of Late Transition Metal Complexes with Flexible Tetra(NHC) Ligands

Daniel T. Weiss, **Philipp J. Altmann**, Stefan Haslinger, Christian Jandl, Alexander Pöthig, Mirza Cokoja, Fritz E. Kühn

One decisive property of many macrocyclic, polydentate ligands is their intrinsic rigidity. To overcome this restriction and introduce a maximum of flexibility, this work deals with the synthesis and characterization of late transitions metal ions complexes open-chain, alkyl-bridged tetra(NHC) ligands.[37] So far, only acyclic systems connected by arene entities were established that are generally unable to chelate metal ions due to their inelastic linkers.

The recently reported silver(I) complexes **21** and **28**[37] were employed as transmetalation agents for the synthesis of a variety of novel compounds targeting unprecedented coordination modes. Upon treatment of complex **21** with halide-based transition metal salts or complexes the metal-exchange reaction readily proceeded in excellent yields (Scheme 42).
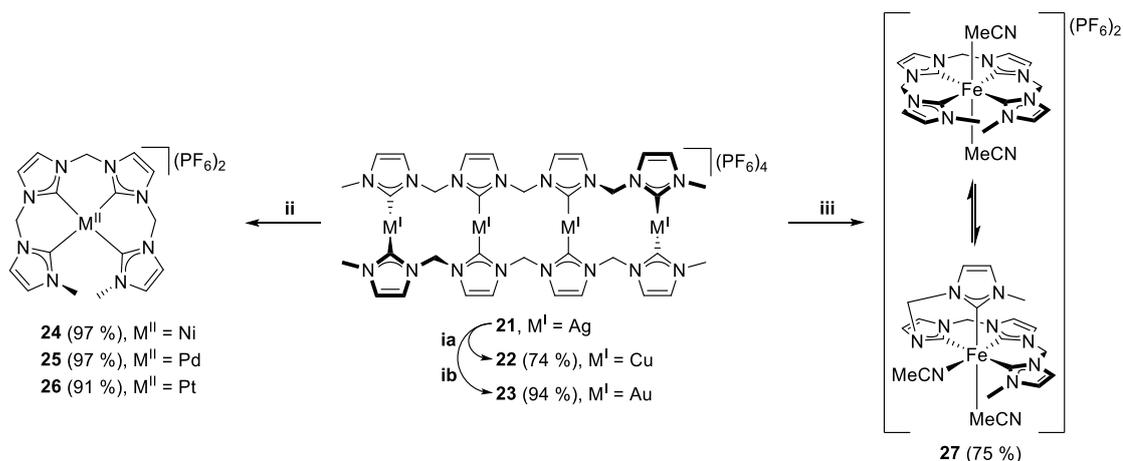
Scheme 42. Transmetalation reactions to metal ions Cu^I, Au^I, Ni^{II}, Pd^{II}, Pt^{II}, and Fe^{II} employing the tetranuclear silver tetra(NHC) complex **21**: (**ia**) CuCl (MeCN), 50 °C, 16 h; (**ib**) [AuCl(SMe$_2$)] (MeCN), 50 °C, 16 h; (**ii**) $M^{II}Cl_2$ (M^{II} = Ni, Pd, Pt), (MeCN), 75-85 °C, 1-5 d; (**iii**) [FeBr$_2$(THF)$_2$], (MeCN), r.t., 16 h.

With the coinage metal ions Cu^I and Au^I the dimeric, tetranuclear complexes **22** and **23** that are isostructural to the starting material **21**, could be obtained. With group 10 metal ions on the other hand, the mononuclear compounds **24**, **25** and **26** resulted with the oligodentate ligand wrapped around the metal centers producing a square-planar coordination motif, as this is the preferred conformation for these ions. In-depth analysis of the coordination geometry generated by the ligand, the complexes' τ values (0 for ideally square-planar, 1 for tetrahedral coordination) were determined.[38] For **24** a τ of 0.23 was found which is lower than those of comparable Ni^{II}(NCCN) systems (0.28 to 0.30),[39] but significantly higher as compared to macrocyclic tetra(NHC) complexes of group 10 ions exhibiting τ values of below 0.10.[1b] For the Pt^{II} analogue

25 a τ of 0.19 was calculated suggesting a slightly more planar coordination behavior as for **26**, whereas suitable single crystals of **25** could not be obtained.

Certainly, the most interesting case is the iron(II) complex **27** as earlier studies involving Fe^{II}(NCCN)-type systems showed structural variability depending on the length of the alkyl linker between the imidazole heterocycles.[40] For **27**, a fluxional behavior of the NHC ligand at room temperature was encountered that can be frozen at -40 °C, where the two different conformers, namely a sawhorse and an equatorial one, are present next to each other (Scheme 42). The respective iron(II) complex with the NHC ligand bound in the equatorial plane could be obtained as the exclusive product by reaction of **27** with an excess of PMe₃ resulting in an irreversible exchange of the MeCN moieties with the stronger coordinating phosphines (Figure 34, left).

31 (95 %), M^{II} = Ni
32 (93 %), M^{II} = Pd
33 (71 %), M^{II} = Pt

28, M^{I} = Ag
ia **29** (59 %), M^{I} = Cu
ib **30** (70 %), M^{I} = Au

34 (87 %)
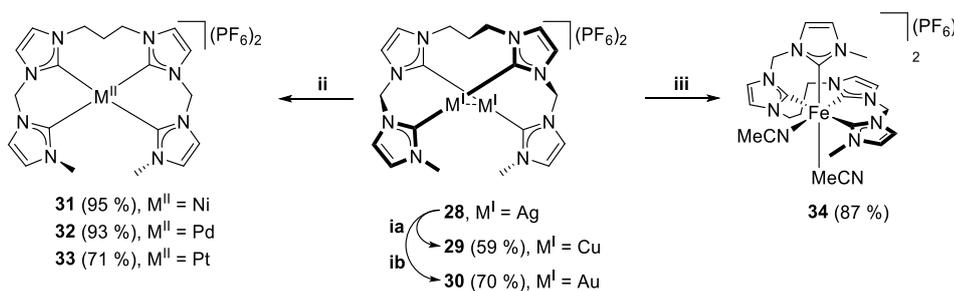
Scheme 43.   Transmetalation reactions to metal ions Cu^{I}, Au^{I}, Ni^{II}, Pd^{II}, Pt^{II}, and Fe^{II} employing the dinuclear silver tetra(NHC) complex **28**: (**ia**) CuCl (MeCN), 50 °C, 16 h; (**ib**) [AuCl(SMe₂)] (MeCN), 50 °C, 16 h; (**ii**) M^{II}Cl₂ (M^{II} = Ni, Pd, Pt), (MeCN), 75-85 °C, 1-5 d; (**iii**) [FeBr₂(THF)₂], (MeCN), r.t., 16 h.

The silver(I) complex **28** was employed in analogous transmetalation reactions (Scheme 43). Its only difference to **21** is the central alkyl chain that is prolonged by two methylene units causing a crucially different coordination motif for linearly coordinated coinage metals. The compounds **29** and **30** are isostructural to **29** and comprise two metal centers bound by two carbon donors each giving rise to very close Au–Au contacts of 2.9676(3) Å in the case of **30**. The molecular structures of the group 10 metal ion complexes **31**-**33** coordinated by this ligand are very similar to those observed for the system with a shorter alkyl bridge. The enhanced flexibility of the propyl bridged carbene ligand leads to a reduced distortion of the square-planar structure, reflected by the τ values of 0.11 for **31** and 0.08 for **32**, respectively.
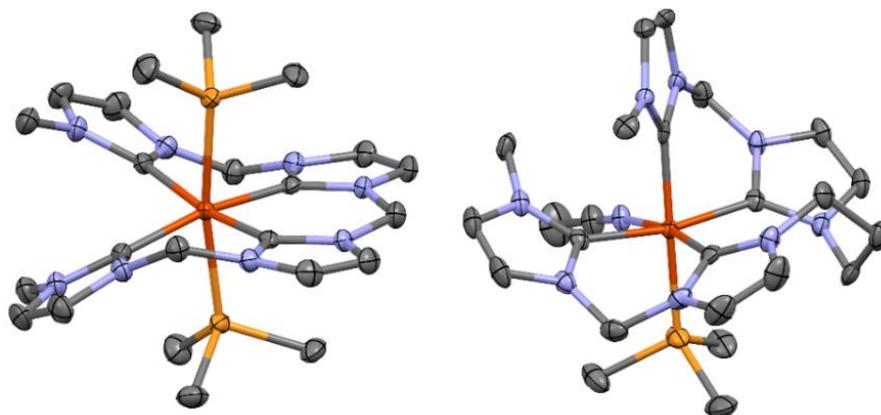
Figure 34.   ORTEP style representation of the dicationic fragments of **27-(PMe₃)₂** (left) and **34-PMe₃** (right) with ellipsoids shown at 50 % probability. Hydrogen atoms, co-crystallized solvent molecules and hexafluoridophosphate anions are omitted for clarity.

In contrast to **27** that shows fluxional behavior in solution, the respective iron(II) complex **34** features an inflexible octahedral coordination of the metal center with two *cis*-acetonitrile ligands and the tetra(NHC) ligand in a sawhorse-type binding mode. Reactions of **34** with excess trimethylphosphine only afforded the mono(PMe$_3$) substituted complex **34-PMe$_3$** with the second acetonitrile entity remaining bound. The sawhorse-type coordination of the tetra(NHC) ligand is retained upon PMe$_3$ introduction (Figure 34, right). The τ values calculated from the molecular structure in the solid state of **34** confirm a classical sawhorse-type coordination of the propyl-bridged ligand, which is the first report of a tetra(carbene) exhibiting such a binding mode within an octahedrally coordinated metal complex.

4.8   Steering Ligands for Catalysts: *N*-heterocyclic Carbenes

Philipp J. Altmann, Korbinian Riener, Fritz E. Kühn, Wolfgang A. Herrmann

In this review that is directed towards a broad readership throughout society interested in chemistry the concept of *N*-heterocyclic carbenes and their application as steering ligands in catalysis and related fields is evaluated. It focusses on the impact of this ligand class on modern chemistry and its properties that led to this tremendous growth in importance over the last two decades. In metal-organic, but also in technical catalytic transformations, phosphines ligands are ubiquitous. However, this class of ligands has a number of inherent disadvantages, most notably their sensitivity towards oxidation.[41] This characteristic can be seen as one of the main reasons for the rise of NHCs as viable steering ligands. One field of application, where NHCs showed superior properties is that of olefin metathesis. Their utilization as steering ligands instead of phosphines led to a higher stability of the catalysts against water and air as well as a higher tolerance for substrates with a variety of functional groups.[41b,42] Two more striking advantages of *N*-heterocyclic carbenes are their ready accessibility and the high stability of the ligand precursors which allows for easy upscaling and storage of these compounds. Throughout the years a plethora of different synthetic approaches for NHC precursors and complexes has been discovered and optimized. Common approaches for the synthesis of metal complexes are amongst others the generation of a free carbene *via* C–H deprotonation and subsequent coordination of a suitable metal center, utilization of metal precursors with an internal base, or the synthesis of the respective silver(I) complex *via* reaction with Ag$_2$O and subsequent transmetalation to another metal ion with precipitation of silver halides.[43] As NHC complexes of transition metals from the middle or late d-block are kinetically very stable, the carbene ligands qualify as steering ligands for molecular catalysts. When optimizing complexes for certain applications, another strong advantage of NHCs becomes apparent: The ligand's properties depend on various factors, which can be influenced independently of each other to a great extent by structural modifications of the heterocyclic scaffold. Amongst the most important setscrews are the number and position(s) of heteroatoms, the nature of the ligands backbone, as well as the steric and electronic influence of different wingtip substituents at the heteroatoms.[44]
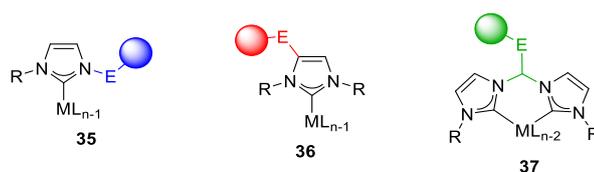
Figure 35.   Different immobilization strategies (**35**-**37**) for NHC complexes (E = alkyl, aryl, ether, amide, ester…). The colored spheres symbolize the solid support.

A major application of NHCs is the development of immobilized catalyst system in order to simplify the catalyst recycling and thereby merge the advantages of both homogeneous and heterogeneous catalysis. Aim of this approach is the anchoring of molecular catalysts on solid carrier materials. For *N*-heterocyclic carbenes three distinct approaches have been developed that utilize different modifications at the ligand framework, exemplified by **35**-**37** (Figure 35).

Against the background of both green and economic process designs it is desirable to use water as solvent. As most NHC complexes are not soluble in an aqueous medium due to their lipophilic characteristics, certain modifications need to be taken into consideration to overcome the hydrophobic tendency. The most common strategy is to install ionic or highly polar functionalities at the ligand's framework, such as carbonate, sulfonate, ammonium, or hydroxyl substituents (**38**-**40**, Figure 36).[45] For catalytic applications this implies usually an easier catalyst separation while maintaining comparable activities.
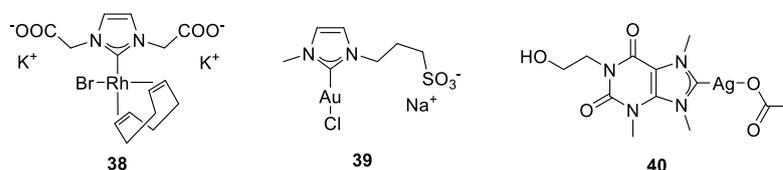
Figure 36.   Examples (**38**-**40**) for hydrophilic NHC complexes with different functionalities. Exemplarily, the solubility of gold complex **39** was found to be 680 mg mL^{-1}.

Another high-potential field is that of asymmetric catalysis, which is of utmost importance for the synthesis of pharmaceuticals or related bio-active compounds. Shortly after the discovery of the catalytic capabilities of NHC complexes, chiral versions have been synthesized and applied. Their common principle is to retain stereo-information introduced by chiral substituents *via* preventing the rotation about the carbene-metal bond (Figure 37).[46] Although this field is still in its infancy, a tremendous progress has been made during the last years.
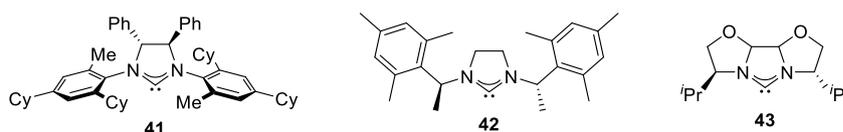
Figure 37.   Examples (**41**-**43**) for chiral imidazolium cations applicable for the synthesis of chiral catalysts.

Apart from the abovementioned a manifold of further applications has been found for these highly versatile compounds. NHCs have been shown to stabilize reactive intermediates due to their strong σ-donating nature, allowing for valuable insights into processes involving such high-valent species.[47] Furthermore, a number of noble metal complexes with hydrophilic NHC ligands have successfully been utilized for medicinal purposes because of their antibacterial and antitumor properties.[29a] Another potential field for NHCs is that of organic light emitting diodes (OLEDs) and artificial photosynthesis, where complexes based on carbene ligation showed very promising results.[29a,48]

4.9   Speciation in Iron Epoxidation Catalysis:
A Perspective on the Discovery and Role of non-heme
Iron(III) Hydroperoxo Species in Iron Catalyzed Oxidation Reactions

Sebastian M. Hölzl,[‡] **Philipp J. Altmann,**[‡] Jens W. Kück, Fritz E. Kühn

[‡] S. M. Hölzl and P. J. Altmann contributed equally to this work.

The understanding of iron cofactors and their role in biological oxidation catalysis are a key target of current research efforts. Over the last 25 years numerous reactive high-valent iron-oxo intermediates were synthesized, isolated and characterized, various reaction pathways discovered, and promising candidates for catalysis evaluated.[49] The discovery of compounds containing the first iron(IV)- and iron(V)-oxo moieties can be seen as milestones within the field.[50] Likewise, iron(III)-hydroperoxo complexes were recognized to be crucial intermediates almost four decades ago, however, they have remained elusive to crystallographic characterization to date. This review comprehensively summarizes the synthesis, reactivity, analytics, as well as the role in catalysis of mononuclear, non-heme iron(III)-hydroperoxo entities as one of the less researched, but still very decisive species of iron-based oxidation chemistry.

Shortly after fundamental investigations of the electronic properties of bleomycin,[51] a non-ribosomal peptide capable of inducing DNA strand breaks upon activation with molecular oxygen, the first simplified model systems were designed in the early 1990s.[52] Based on these results and the prediction of Valentine *et al.* in 1991 that iron(III)-hydroperoxo species are involved during the catalytic epoxidation of alkenes,[53] a variety of further ligand systems was designed enabling the synthesis of Fe^{III}-OOH complexes *via* different approaches (Scheme 44).

$$LFe^{II} + O_2 + e^- + H^+$$

$$LFe^{II} + 1.5\ H_2O_2 \xrightarrow[-H_2O]{} \boxed{LFe^{III}\text{-OOH}} \longleftarrow LFe^{II} + O_2^- + H^+$$

$$LFe^{II}\text{-}\eta^2\text{-}O_2 + H^+$$
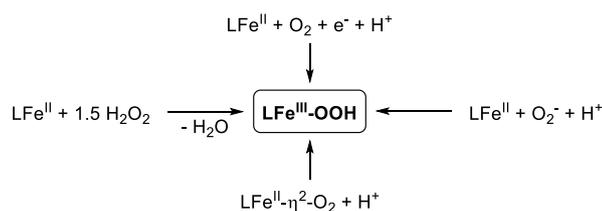
Scheme 44.   Schematic synthetic routes toward iron(III)-hydroperoxo complexes.

The most common route for their synthesis is the reaction of a suitable iron(II) complex with an excess of hydrogen peroxide as aqueous solution of different concentrations. In general, the intensely purple colored solutions of *in situ* generated Fe^{III}-OOH entities are characterized or further reacted directly from these mixtures, albeit their isolation has been reported in rare cases.[54] It showed that the hydroperoxo species forms more rapidly at elevated temperatures, which in turn also leads to higher degradation rates.[55] The highest amount of hydroperoxo entity is obtained a few minutes after addition of H_2O_2 to the iron(II) precursor in most cases before its decay prevails.[56] Another approach for the synthesis of these iron(III) hydroperoxo species relies on the reaction of a Fe^{II} complex with molecular oxygen in the presence of protons and a reducing agent,

such as 1-benzyl-1,4-dihydronicotinamide (BNAH)[57] or tetraphenylborate.[58] Additionally, the Fe^{III}-OOH moiety can be generated by reacting an iron(II) complex with superoxides[59] or from Fe^{III}-η^2-O$_2$ complexes,[60] both under acidic conditions.

The iron(III)-hydroperoxo complexes can be characterized by a plethora of suitable analysis methods. The hydroperoxo complexes display a very prominent absorption band with a maximum between 480 and 590 nm with extinction coefficients of approximately 1000 M^{-1} cm^{-1} and can therefore easily be recognized by their characteristic UV/Vis spectrum.[61] In order to gain insight into the electronic nature of the iron center, EPR spectroscopy is employed. The iron(III) ion can either be in a low-spin S = 1/2 or a high spin S = 5/2 state, giving rise to fundamentally different EPR spectra.[54a,59,61a,61b] Raman spectroscopy provides very useful information about the iron(III)-hydroperoxo species itself. In the spectra of low-spin Fe^{III}-OOH complexes, vibrations at frequencies at approximately 600 and 800 cm^{-1} are observed that are assignable to ν(Fe–O) and ν(O–O). These two bands are highly sensitive toward isotope labelling of the hydroperoxo ligand.[62] Other analysis methods, such as Mössbauer,[51b,63] or EXAFS spectroscopy[60-61,64] have been applied successfully for a deeper insight into the properties of the hydroperoxo complex.

The diversified reactivity of iron(III)-hydroperoxo intermediates plays a key role for oxidation catalysis. They potentially oxidize substrates directly or first undergo heterolytic or homolytic cleavage of the O–O bond to give a high-valent iron-oxo intermediate, respectively. The most determining factor for the reaction pathway is the number and relative position of vacant or labile coordination sites that can readily be influenced by ligand design measures. For pentadenate ligands only one coordination site is open at the iron center which is subsequently occupied by the OOH ligand. Therefore, the substrate does not bind directly to the metal, but rather reacts with the oxo-ligand generated by homolytic O–O cleavage. For tetradentate ligand systems affording *cis*-labile coordination sites the picture is more complex. The reaction pathway depends heavily on the reaction conditions applied, specifically on the presence or absence of water.
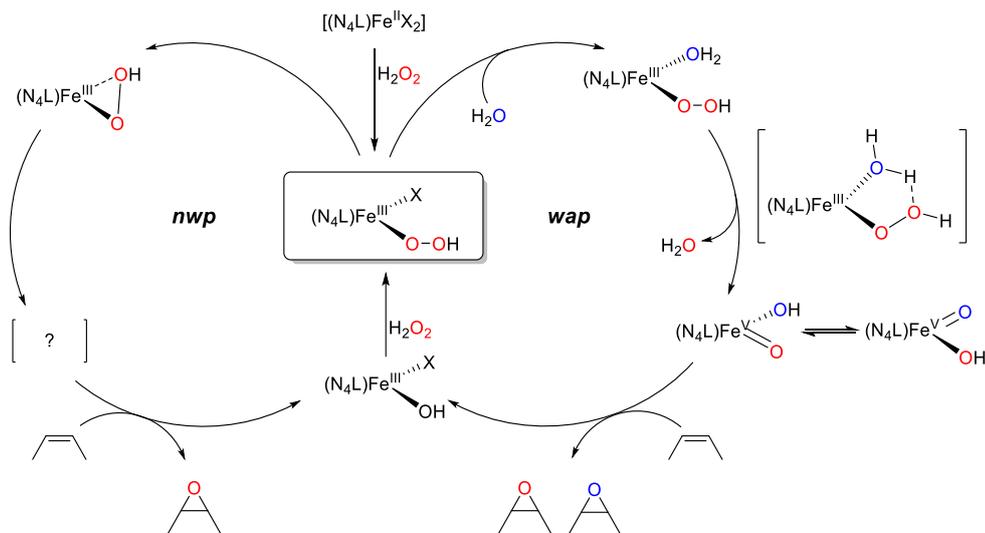
Scheme 45. Non-water-assisted (*nwp*) and water-assisted reaction pathway (*wap*) of alkene epoxidation from a common iron(III)-hydroperoxo complex. The tetradentate ligand is abbreviated as N$_4$L.

In the first case, a *cis*-Fe^{V}(O)(OH) intermediate is believed to form *via* O–O bond heterolysis (*wap*, water-assisted pathway),[65] whereas such a pathway is energetically disfavored without water in the mixture (*nwp*, non-water-assisted pathway).[65b] An O–O bond homolysis is discarded as well, since epoxidation and *cis*-dihydroxylation occur stereospecifically.[65c,66] Instead a Fe^{III}-η^2-OOH moiety is postulated,[65b] but the overall pathway remains elusive due to the lack of conclusive evidence.[67] Additionally, it was shown that the addition of acetic acid as an additive has remarkable effect on the behavior of non-heme iron complexes towards alkenes,[68] due to the formation of a highly electrophilic and epoxide selective Fe^{V}(O)(OAc) intermediates.[65c,69] The third family is that of non-heme iron complexes with *trans*-labile coordination sites. In their case water binding cannot occur proximally to the hydroperoxo ligand and a water-assisted heterolytic O–O bond cleavage is therefore not feasible leading to the formation of a Fe^{IV}=O rather than a Fe^{IV}(O)(OH) complex.[70]

Although the efficient usage of molecular oxygen as terminal oxidant is still elusive, bio-inspired non-heme iron catalysts in combination with H_2O_2 have emerged as versatile tools toward the regio- and stereoselective oxidation of alkenes. As it was shown that efficient epoxidation catalysts generally require two labile coordination sites, pentadentante ligand scaffolds are strongly disfavored for this purpose.[71] For tetradentate ligand motifs with *cis*-labile coordination sites olefin-dihydroxylation is a major reaction. The epoxide to diol ratios (E/D) can be influenced by modifications that influence the steric and electronic situation at the metal center.[72] As mentioned above, the addition of acid additives was shown to remarkably improve both the yield of and selectivity for epoxide over dihydroxide.[68] Based on these reports, a plethora of non-heme ligand systems for asymmetric epoxidation was developed.[73] Nearly quantitative epoxide yields at enantiomeric excesses of up to 98 % have been achieved in certain cases after thorough fine-tuning.[74] In contrast, tetradentate, *trans*-labile sites allow for exclusive epoxidation and therefore give rise to high selectivities without the need for additives as is the case for *cis*-labile complexes.[75] In recent years, NHC-based iron systems were shown to epoxidize olefins with exceptionally high activities.[76]

The progress that has been made in this field over the last decade is remarkable. The hydroperoxo entity was proven to undoubtedly be a crucial part of oxidation catalysis in nature and model systems. Hence, understanding its properties and reactivity helped tremendously to understand processes in catalytic oxidations and to design highly active and selective catalysts for epoxidation, hydroxylation and C–H activation. However, the crystallographic evidence of this entity is still elusive. Additionally, the ultimate goal – employing molecular oxygen as terminal oxidant – is still very much in its infancy. Also catalyst stabilities under oxidizing conditions need to be improved significantly to enable efficient catalyst recycling.

4.10 Reprint Permissions

4.10.1 Introducing a Pyrazole/Imidazole Based Hybrid Cyclophane:
A Hydrogen Bond Sensor and Binucleating Ligand Precursor

4.10.2 Capsoplexes: Encapsulating Complexes *via* Guest Recognition

4.10.3 A hybrid Imidazolylidene/Imidazolium Nickel NHC Complex – An isolated Intermediate

4.10.4 Pillarplexes: A Metal-Organic Class of Supramolecular Hosts

4.10.5 A pH-Dependent, Mechanically Interlocked Switch: Organometallic [2]Rotaxane vs. Organic [3]Rotaxane

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4.10.6 Exploring Coordination Modes: Late Transition Metal Complexes with a Methylene-bridged Macrocyclic Tetra(NHC) Ligand

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4.10.7 Structural Diversity of Late Transition Metal Complexes with Flexible Tetra(NHC) Ligands

4.10.8 Steering Ligands for Catalysts: *N*-heterocyclic Carbenes

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4.10.9 Speciation in Iron Epoxidation Catalysis:

A Perspective on the Discovery and Role of non-heme
Iron(III) Hydroperoxo Species in Iron Catalyzed Oxidation Reactions

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5 BIBLIOGRAPHIC DETAILS
for Complete Publications

5.1 Introducing a Pyrazole/Imidazole Based Hybrid Cyclophane: A Hydrogen Bond Sensor and Binucleating Ligand Precursor

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5.2   Capsoplexes: Encapsulating Complexes *via* Guest Recognition

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5.3 A hybrid Imidazolylidene/Imidazolium Nickel NHC Complex – An isolated Intermediate

Philipp J. Altmann, Michael Ehrenreich, Alexander Pöthig*

Acta Crystallographica **2017**, C73, 880-884

Catalysis Research Center & Department of Chemistry, Technische Universität München, Ernst-Otto-Fischer-Str. 1, 85747 Garching bei München, Germany.

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5.4   Pillarplexes: A Metal-Organic Class of Supramolecular Hosts

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5.5   A pH-Dependent, Mechanically Interlocked Switch: Organometallic [2]Rotaxane vs. Organic [3]Rotaxane

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5.6   Exploring Coordination Modes: Late Transition Metal Complexes with a
Methylene-bridged Macrocyclic Tetra(NHC) Ligand

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5.7 Structural Diversity of Late Transition Metal Complexes with Flexible Tetra(NHC) Ligands

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5.8   Steering Ligands for Catalysts: *N*-heterocyclic Carbenes

Original Title: Steuerliganden für Katalysatoren: *N*-Heterocyclencarbene

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5.9   Speciation in Iron Epoxidation Catalysis:
A Perspective on the Discovery and Role of non-heme
Iron(III) Hydroperoxo Species in Iron Catalyzed Oxidation Reactions

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6 SUMMARY & OUTLOOK

The initial aim of this work was the synthesis and characterization of novel macrocyclic hybrid pyrazole/imidazolium scaffolds as precursors for multinuclear NHC complexes. A successful synthetic route was designed based on a cyclization protocol of a bis(imidazole) bridged by an *N*-protected pyrazole unit (**3**) with methylene bis(trifluoromethanesulfonate) in very diluted solutions at low temperatures (Scheme 46). This approach showed a high selectivity for the desired cyclophane and after a workup procedure that involved *N*-deprotection and separation of minor side-products, such as oligomers and higher macrocycles, the proligand **4-OTf** was obtained in yields of up to 64 % – an excellent value for these type of statistical macrocyclization reactions. The tetra(imidazolium) salt exhibits very promising hydrogen bond sensing properties heavily depending on the counterions present. With weaker coordinating anions, such as PF_6^-, very defined and strong interactions with suitable guest molecules were observed. At the same time the cyclophane **4-PF₆** served as binucleating ligand precursor for Ni^II NHC complexes (Scheme 46). Compound **5** is intrinsically very stable against air and moisture and its bowl-shaped structure is very rigid such that no flipping to a chair-conformation occured, not even at elevated temperatures.
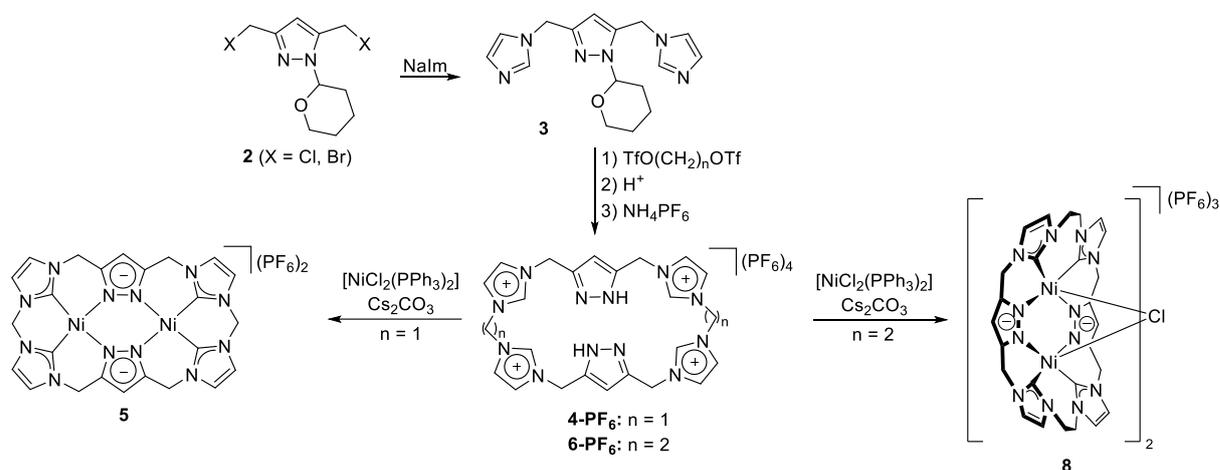
Scheme 46. Synthesis of imidazolium salts **4-PF₆** and **6-PF₆** *via* the general approach developed during this work and their diverse reactivities with [NiCl₂(PPh₃)₂] in the presence of Cs₂CO₃.

Based on these fundamental results, the ligand scaffold was modified by increasing the length of the alkyl linker between the imidazole entities by one CH₂ unit. This seemingly minor change in the periphery of the system was found to have a crucial influence in the curvature of the corresponding dinuclear Ni^II complex. The void is more pronounced as in the methylene-bridged congener and additionally two H-atoms of each of the two ethylene bridges are directed into the half-bowl cavity of the complex. These two features cause this complex to have a highly selective affinity for chloride and bromide anions. The halides are encapsulated in a tennis-ball-like fashion by two symmetry-equivalent cationic Ni₂L complexes forming a so-called "capsoplex" – an unprecedented encapsulation mechanism where the guest plays an active role in the formation of the assembly. Further research efforts have been made in the direction of mixed metal NHC complexes based on this binucleating ligand motif. During the course of these studies it became obvious that the synthesis of hybrid imidazolium/imidazolylidene Ni₃L₂Cl₂-type complexes is possible in case substoichiometric amounts of metal precursor and base are employed in combination with the imidazolium salt.

A topic that was only examined superficially is the electrocatalytic reduction of CO_2 catalyzed by the Ni_2L-type NHC complexes. For that, a number of ligand modifications were screened, such as different linker lengths, or an exchange of the pyrazole by the isoelectronic triazole heterocycle. Preliminary investigations revealed that all analogues are active CO_2 reducing catalysts, however, high negative potentials of approximately -3 V are required for the generation of the catalytically active Ni^I species (Figure 38). The Ni_2L congener featuring propyl-bridged imidazolylidenes and triazolates was found to be the most active catalyst amongst the tested compounds. These proof-of-principle results are certainly very promising, but further ligand tuning is most definitely required in order to drastically reduce the potential at which the catalysts are active.
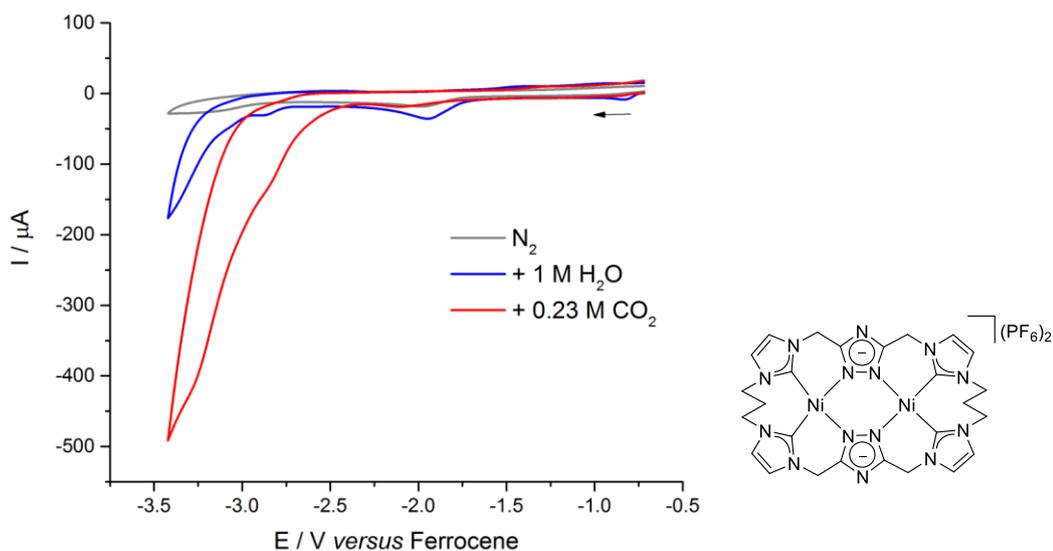
Figure 38.   Left: Representative cyclic voltammograms of the Ni_2L-type complexes, measured under N_2, then after addition of 1 M H_2O, and again after addition of 0.23 M CO_2. Right: Most active catalyst amongst the tested entities.

The second major goal of this thesis project was the synthesis and evaluation of the respective coinage metal (Ag, Au) NHC complexes featuring the established macrocyclic ligand motif. The reaction of the proligand salt with silver(I) oxide readily afforded the desired product in good yield after a straightforward and facile workup procedure. Employing the complex as carbene transfer reagent in combination with [AuCl(SMe$_2$)] yielded the isostructural gold congener (Scheme 47).
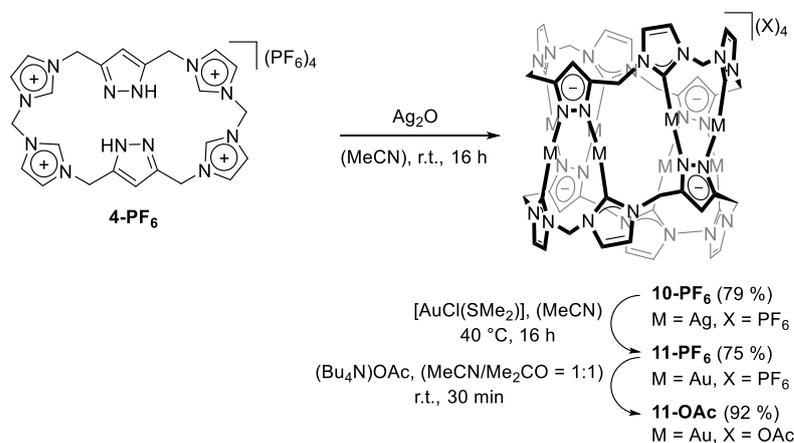
Scheme 47.   Synthesis of pillarplexes **10-PF₆**, **11-PF₆** and **11-OAc**.

Both complexes are composed of two ligand molecules bridged by eight metal centers coordinated linearly between them. This leads to a very rigid cylinder-shaped structure with a defined tubular cavity in its center rendering the complexes referred to as "pillarplexes" a rare example of a metallocavitand able to act as a host for supramolecular interactions. It could be shown that the pillarplexes' unique prerequisite of their void leads to several properties highly beneficial for "chemistry beyond the molecule" (Figure 39). Their solubility can be influenced significantly by simple anion exchange reactions, such that even water-soluble analogues were obtained. Additionally, the cavity shows an exclusive size selectivity for linear over six-membered aromatic molecules, which is a unique characteristic of this compound class, as all other organic architectures host either both or none of these. On top of that, the Au_8 compounds show a high intrinsic photoluminescence in the blue region of the visible spectrum upon UV irradiation. In the presence of luminescence quenching guests this feature can be used for quantification purposes. In comparison to established organic host molecules, such as the structurally comparable pillar[5]arene, the pillarplex shows higher association constants.
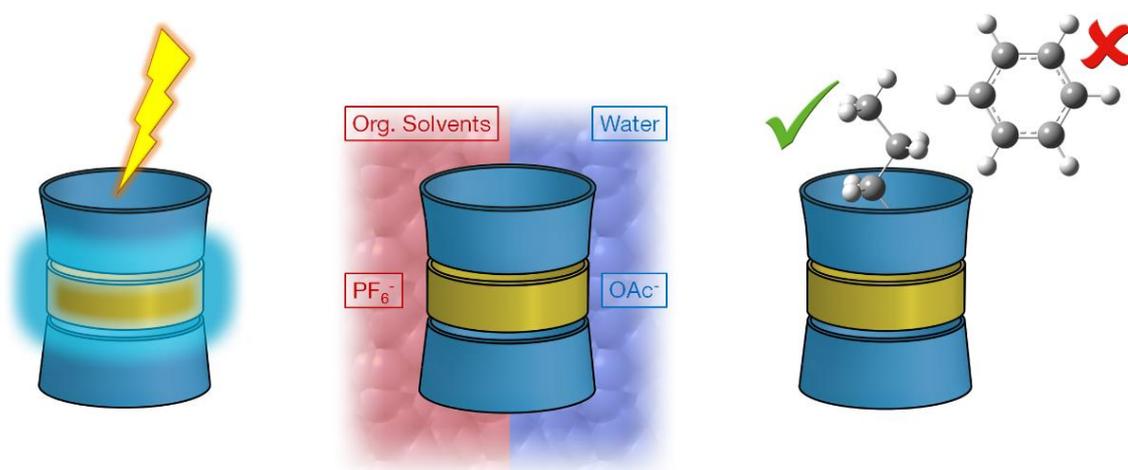
Figure 39. Graphical representation of the Au_8-pillarplex's key features. Left: UV-triggered, quenchable luminescence. Middle: Easily tunable solubility *via* anion exchange reactions. Right: Size and shape selectivity caused by the unique steric prerequisites of the pillarplex's cavity.

With these results as the cornerstone a series of further developments can be envisioned. Exemplarily, an exchange of the alkyl bridges between the imidazole heterocycles by dialkylborates entities should lead to several beneficial properties. That way, each pillarplex molecule would contain four additional negative charges (one per borate linker). In addition to the four negative charges of the pyrazolate binding sites the charge of the eight M^I (M = Ag, Au) should be compensated and the pillarplex entity would be overall neutral (Scheme 48).
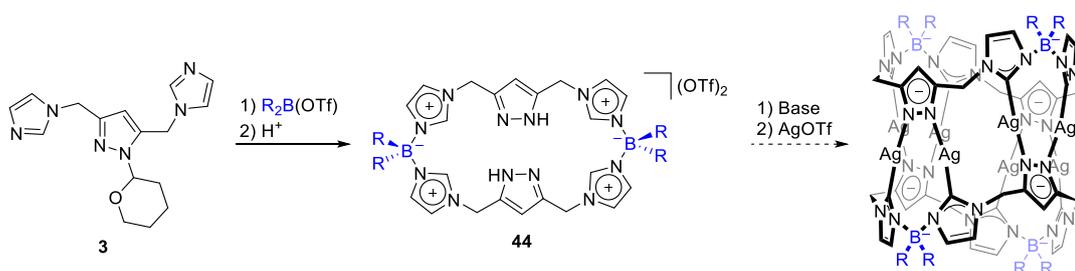
Scheme 48. Envisioned ligand motif with borate-based bridging moieties potentially yielding neutral pillarplexes.

This would allow for complementary host-guest applications of this borate-based compound in more apolar solvents, such as toluene or dichloromethane, wherein the standard alkyl-bridged pillarplexes are not soluble. Moreover, the borate moiety allows for a delicate steric and electronic modification by variation of its two additional substituents in the ligand's periphery. The feasibility of the borate-bridged imidazolium salt **44** could already be demonstrated by first proof-of-principle experiments. The desired ring size is readily obtained *via* a cyclization procedure analogous to the approach for the alkyl-bridged imidazolium salts, such as **4-OTf**. Problematic with the resulting macrocyclic entities is the fact that the cleavage of the tetrahydropyranyl protection group is generally performed in the acidic milieu. This needs to be brought into agreement with the borate moieties that tend to be hydrolyzed under such conditions. However, initial experiments employing anhydrous triflic acid yielded promising results and small amounts of the deprotected cyclophane were obtained exhibiting a good purity. Analysis by NMR spectroscopy and MS spectrometry suggested the formation of the dicationic imidazolium salt. Additionally, single crystals could be grown and a preliminary solid state structure was obtained proving the correct connectivity and overall charge of the potential proligand (Figure 40). However, no studies in terms of its reactivity have been carried yet, but are expected to yield neutral pillarplexes isostructural to **10** and **11**.
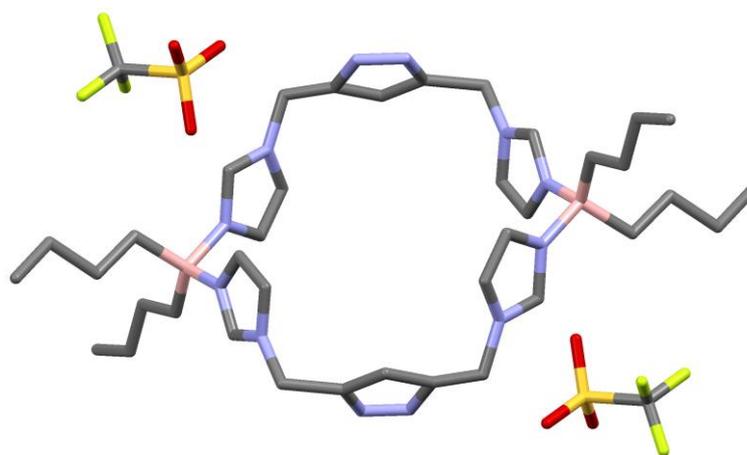
Figure 40.   Preliminary solid state structure of the hybrid imidazolium/pyrazole cyclophane featuring dibutylborate bridging moieties between the imidazolium heterocycles. The presence of only two triflate anions per macrocyclic cation proves its reduced charge compared to **4**.

Another valid possibility to further functionalize the ligand scaffold is by modifying the backbone positions of either the pyrazole or imidazole entities. However, initial experiments revealed that the pillarplex formation is very sensitive towards variations especially of the imidazoles' C4 and C5 positions. Initially, this strategy was pursued as the respective ligand precursors are easily accessible by variation of the imidazolide that is used for the synthesis of the cyclization precursor **3**. Exemplarily, the calix[4]4,5-dimethylimidazolium[2]pyrazole salt was obtained *via* reacting the di(chloromethyl)pyrazole derivative **2-Cl** with sodium 4,5-dimethylimidazolide and subsequent cyclization reaction with $CH_2(OTf)_2$. However, the reaction of the proligand with Ag_2O did not yield an analogous Ag_8L_2 pillarplex but rather an $Ag_{11}L_3$-type complex due to steric repulsion of the methylated backbone moieties of the imidazolylidenes (Figure 41). This structural motif is highly interesting in terms of metal–metal interactions, as it exhibits some very short Ag–Ag distances as low as 2.728 Å. Therefore, the Au_{11} analogue should be prepared and tested for its emissive properties. In turn, this structure is not

applicable for host-guest applications because this coordination motif does not allow for a cavity within the structure (Figure 41). Thus, a changes in the pyrazole's backbone seems a more promising approach for ligand modifications while retaining the M_8L_2 scaffold.
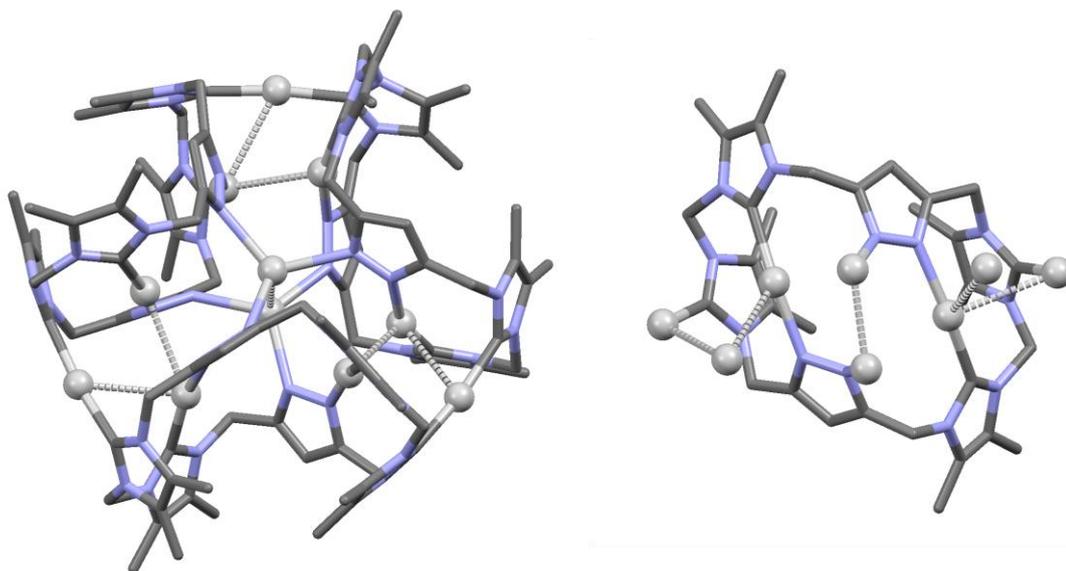
**Figure 41.**   Left: Preliminary solid state structure of $[Ag_{11}L_3]^{5+}$-type complex obtained from reaction of the calix[4]4,5-dimethyl-imidazolium[2]pyrazole proligand with Ag_2O. Right: Cutout of the structure with only one ligand molecule and its unconventional coordination pattern shown. The structures are depicted in capped sticks with the silver(I) ions as balls. Hydrogen atoms, counterions and co-crystallized solvent molecules have been omitted for clarity.

Inspired by the recent development within the area of mechanomolecules, the pillarplexes were employed for the synthesis of [2]rotaxane assemblies. Due to the high association constants between the organometallic Ag_8 host and the axle compound 1,12-diaminodecane, the respective mechanically interlocked molecule was obtained in nearly quantitative yield after stoppering with 3,5-di-*tert*-butylbenzoic anhydride in the presence of a base. In contrast to virtually all other host compounds employed for this purpose, the pillarplex exhibits a high post-synthetic modifiability, such that the silver centers are still capable of carbene transfer, exemplarily demonstrated by the synthesis of the Au_8 analogue *via* transmetalation. Additionally, the host complex could be decomposed by addition of strong acids, resulting in a purely organic [3]rotaxane. As this reaction is reversible upon addition of a suitable base, the assembly can be understood as pH-dependent switch. During these investigations it became clear that the mechanically interlocked nature of the system leads to a kinetic stabilization of the NHC complex in a way that harsher conditions are necessary for its degradation. This behavior is well-known for related catenanes coordinated to metal ions, but has never been observed within a rotaxane scaffold before. Thus, the term "rotaxand-effect" was coined in accordance to the established catenand-effect.

The beauty of the mechanically interlocked design of this architecture lies within its modularity. In principle, a manifold of functionalities can be attached to the pillarplex by simple amidation reactions with a hosted diamine moiety. Exemplarily, complexes containing both coordinated gold(I) centers as well as redox-active species, such as the reversible Fe^{II}/Fe^{III} couple in ferrocenes, have recently been shown to be potential so-called dual-approach anticancer agents: Gold(I) is able to selectively inhibit the enzyme thioredoxin reductase, an essential enzyme that is

often overexpressed in cancer cells. Additionally, the generation of reactive oxygen species by redox-active substances leads to apoptosis of affected cells in case their level surpasses a certain limit. Whereas normal cells are believed to have a greater capacity for adaption, cancerous cells are very sensitive in that context.

Thus, combining both of these concepts might results in cooperative effects in cancerous cells and allow for effective anti-cancer agents. At this point, it was possible to obtain the gold-based [2]rotaxane stoppered by ferrocene entities. Upon subsequent anion exchange to acetates, the highly water-soluble compound **45** was obtained and is currently being tested for its antitumor behavior (Figure 42, left).
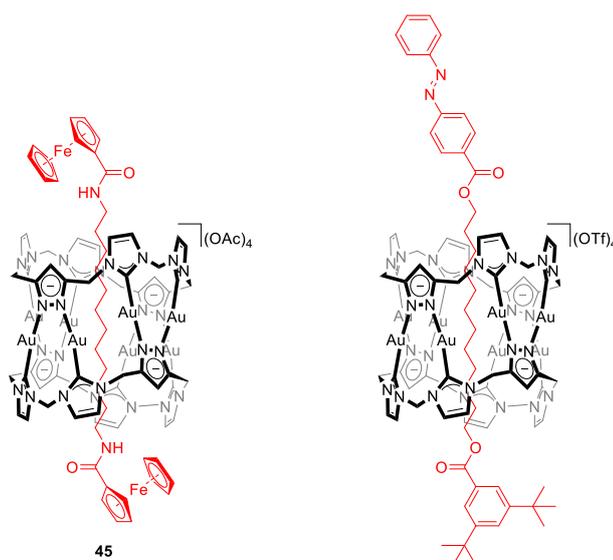

Figure 42.   Potential modifications based on the [2]rotaxane architecture towards different applications: Left: Ferrocene-stoppered Au_8-[2]rotaxane for an dual-approach strategy against cancer cells. Right: "Rotopillar" assembly designed as undirected molecular motor relying on continuous E/Z isomerization of the N=N double bond triggered by UV irradiation and the subsequent blue luminescence from the Au_8 host.

Moreover, the installation of an azobenzene entity as stopper could allow for the design of a simple molecular rotor driven by a continuous E/Z isomerization of the N=N double bond by external UV light and simultaneously occurring blue emission of the pillarplex (Figure 42, right). Given that this motion is fast enough for the whole [2]rotaxane to overcome the chaotic effect of Brownian motion, the (statistical) motion of the assembly should allow for it to move from an illuminated to a dark area and accumulate there. Another highly interesting question is whether it is possible to employ the Ag_8-based [2]rotaxane as transmetalation agent for the synthesis of non-isostructural complexes. This could lead to exciting and potentially novel coordination motifs of the cyclophane, as the axle threaded through the macrocycle prevents certain coordination geometries.

Under the general theme "*N*-heterocyclic carbenes", some further investigations not related to the hybrid pyrazole/imidazole system were conducted. First, a similar ligand, namely a cyclophane containing four methylene-bridged imidazole heterocycles as the exclusive donor sites was employed for the synthesis of the tetranuclear silver(I) NHC complex (Figure 43, left). By using this compound as carbene transfer agent the respective NHC complexes with Ni^{II}, Pd^{II}, Pt^{II}

and Au^I as metal centers could be obtained. The isostructural gold(I) complex shows photoluminescence in the blue visible region with a quantum yield around 30 %. The group 10 metal ions form square planar mononuclear complexes with all four carbene donors bound to them. To gain a deeper insight into the structural properties of the ML-type complexes, the ligands' fluxional behavior was studied by means of spectroscopy and DFT calculations revealing significant differences depending on the size of the metal center.
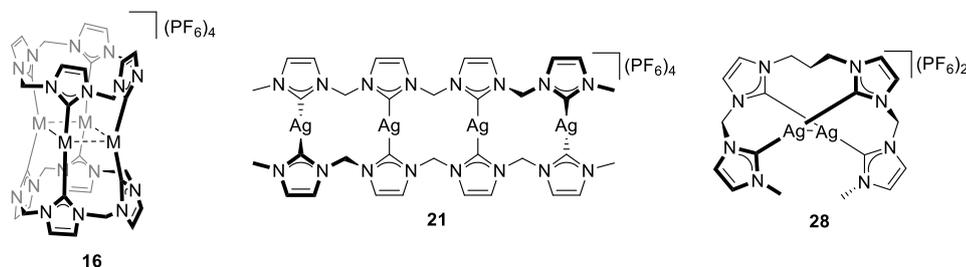
Figure 43.   Investigated silver(I) complexes of macrocyclic and open-chain tetra(NHC) ligands.

Analogously, the coordination chemistry of different open chain tetra(NHC) complexes obtained by carbene transfer from **21** and **28** was examined (Figure 43, middle and right). The Fe(II) complex **27** was of particular interest as it was found to exhibit a dynamic ligand behavior that could be inhibited by phosphine coordination.

Apart from the results based on own research presented in this thesis a review article was prepared dealing with the chemistry of iron(III) hydroperoxo complexes in the context of oxidation catalysis. Therein, iron NHC are described briefly as highly active epoxidation catalysts. Another review article directed to a broad audience of general chemical interest comprises a comprehensive description of *N*-heterocyclic carbenes and their role as steering ligands in catalysis and related applications.

7 APPENDIX

7.1 Complete List of Publications

7.1.1 Journal Contributions

[20] *High-Melting, Elastic Polypropylene:*
A One-Pot, One-Catalyst Strategy toward Propylene-Based Thermoplastic Elastomers
M. R. Machat, D. Lanzinger, M. Drees, **P. J. Altmann**, E. Herdtweck, B. Rieger
Macromolecules **2018**, *51*, 914-929.

[19] *Synthesis, Characterization and Derivatization of*
Hydroxyl-functionalized Iron(II) bis(NHC) Complexes
A. C. Lindhorst, M. Kaspar, **P. J. Altmann**, A. Pöthig, F. E. Kühn
Dalton Transactions **2018**, *47*, 1857-1867.

[18] *Silicon and Oxygen's Bond of Affection:*
An Acyclic Three-Coordinate Silanone and its Transformation to an Iminosiloxysilylene
D. Wendel, D. Reiter, A. Porzelt, **P. J. Altmann**, S. Inoue, B. Rieger
Journal of the American Chemical Society **2017**, *139*, 17193-17198.

[17] *A pH-Dependent, Mechanically Interlocked Switch:*
Organometallic [2]Rotaxane vs. Organic [3]Rotaxane
P. J. Altmann, A. Pöthig
Angewandte Chemie International Edition **2017**, *56*, 15733-15736.
Angewandte Chemie **2017**, *129*, 15939-15942.

[16] *A hybrid Imidazolylidene/Imidazolium Nickel NHC Complex – An isolated Intermediate*
P. J. Altmann, M. Ehrenreich, A. Pöthig
Acta Crystallographica **2017**, *C73*, 880-884.

[15] *Speciation in Iron Epoxidation Catalysis: A Perspective on the Discovery and Role of non-heme*
Iron(III) Hydroperoxo Species in Iron Catalyzed Oxidation Reactions
S. M. Hölzl,[‡] **P. J. Altmann**,[‡] J. W. Kück, F. E. Kühn
Coordination Chemistry Reviews **2017**, *352*, 517-536.

[14] *A Stable Neutral Compound with an Aluminum-Aluminum Double Bond*
P. Bag, A. Porzelt, **P. J. Altmann**, S. Inoue
Journal of the American Chemical Society **2017**, *139*, 14384-14387.

[13] *A macrocyclic 'Co0' complex: the relevance of ligand non-innocence to reactivity*
M. Kaspar, **P. J. Altmann**, A. Pöthig, S. Sproules, C. R. Hess
Chemical Communications **2017**, *53*, 7282-7285.

[12] *Mannich N-Indolylmethylation of Amino Acids*
M. Wiedemann, **P. J. Altmann**, L. Hintermann
Synthesis **2017**, *49*, 2257-2265.

[11] *Synthesis of Tetraoxygenated Terephthalates via a Dichloroquinone Route:*
Characterization of Cross-Conjugated Liebermann Betaine Intermediates
L. Hintermann, **P. J. Altmann**, P. Naumov, K. Suzuki
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[10] *Pillarplexes: A Metal−Organic Class of Supramolecular Hosts*
P. J. Altmann, A. Pöthig
Journal of the American Chemical Society **2016***, 138,* 13171-13174.

[9] *Self-assembled palladium and platinum coordination cages:*
Photophysical studies and anticancer activity
F. Kaiser, A. Schmidt, W. Heydenreuter, **P. J. Altmann**, A. Casini, S. A. Sieber, F. E. Kühn
European Journal of Inorganic Chemistry **2016**, *33*, 5189-5196.

[8] *Exploring coordination modes:*
Late transition metal complexes with a methylene-bridged macrocyclic tetra-NHC ligand
P. J. Altmann, D. T. Weiss, C. Jandl, F. E. Kühn
Chemistry – An Asian Journal **2016**, *11*, 1597-1605.

[7] *Capsoplexes: Encapsulating Complexes via Guest Recognition*
P. J. Altmann, A. Pöthig
Chemical Communications **2016**, *52*, 9089-9092.

[6] *Six- and seven-coordinate Fe(II) and Zn(II) Compounds ligated by unsymmetric Xanthene-based*
Ligands: Characterization and magnetic Properties
R. M. Haas, M. Arshad, J. Anthony, **P. J. Altmann**, A. Pöthig, F. H. Köhler, C. R. Hess
Inorganic Chemistry Frontiers **2016**, *3*, 616-629.

[5] *Structural Diversity of Late Transition Metal Complexes with Flexible Tetra-NHC Ligands*
D. T. Weiss, **P. J. Altmann**, S. Haslinger, C. Jandl, A. Pöthig, M. Cokoja, F. E. Kühn
Dalton Transactions, **2015**, *44*, 18329-18339.

[4] *Maßgeschneiderte Steuerliganden für Katalysatoren am Beispiel der N-Heterocyclencarbene*
P. J. Altmann, K. Riener, F. E. Kühn, W. A. Herrmann
Chemie in unserer Zeit **2015**, *49*, 260-269.

[3] *Introducing a Pyrazole/Imidazole Based Hybrid Cyclophane:*
     A Hydrogen Bond Sensor and Binucleating Ligand Precursor
     P. J. Altmann, C. Jandl, A. Pöthig
     Dalton Transactions **2015**, *44*, 11278-11281.

[2] *Spectroscopic and Structural Properties of Bridge-Functionalized Dinuclear Coinage-Metal (Cu, Ag,*
     and Au) NHC Complexes: A Comparative Study
     R. Zhong, A. Pöthig, D. C. Mayer, C. Jandl, **P. J. Altmann**, W. A. Herrmann, F. E.
     Kühn
     Organometallics **2015**, *34*, 2573-2579.

[1] Synthesis and Comparison of Transition Metal Complexes of Abnormal and Normal
     Tetrazolylidenes: A Neglected Ligand Species
     L.-A. Schaper,[‡] X. Wei,[‡] **P. J. Altmann**, K. Öfele, A. Pöthig, M. Drees, J. Mink, E.
     Herdtweck, B. Bechlars, W. A. Herrmann, F. E. Kühn
     Inorganic Chemistry **2013**, *52*, 7031-7044.

[‡] Equally contributing co-authors.

7.1.2 Conference Contributions

- **P. J. Altmann**, C. Jandl, A. Pöthig
  Poster, ChemKrist Workshop, Frankfurt/Main 2015

- **P. J. Altmann**, A. Pöthig
  Talk, 24th annual meeting of the Deutsche Gesellschaft für Kristallographie, Stuttgart 2016.

- **P. J. Altmann**, A. Pöthig
  Poster, 24th annual meeting of the Deutsche Gesellschaft für Kristallographie, Stuttgart 2016.

- **P. J. Altmann**, A. Pöthig
  Poster, RSC Macrocyclic and Supramolecular Chemistry Meeting, Edinburgh, UK 2016.

- **P. J. Altmann**, A. Pöthig
  Poster, 25th annual meeting of the Deutsche Gesellschaft für Kristallographie, Karlsruhe 2017.

- **P. J. Altmann**, A. Pöthig
  Poster, 253rd National Meeting of the American Chemical Society, San Francisco, USA 2017.

- **P. J. Altmann**, A. Pöthig
  Poster, Workshop (TUM-IAS & UoB-IAS) "Inorganic Chemistry meets Medicine", Munich 2017.

7.2 Contribution to individual Publications

Table 4. Contribution of Ph.D. candidate P. J. Altmann to individual publications (‡ = equally contributing as first author, exp. = experimental, ana. = analytical).

Bibliographic Data	Chapter	Author	Contribution
Dalton Trans. **2015**, *44*, 11278-11281	4.1	1st	support with conceptual approach, exp. work (excluding XRD), DFT study, co-conception and co-writing of manuscript
Chem. Commun. **2016**, *52*, 9089-9092	4.2	1st	support with conceptual approach, exp. and ana. work, co-conception and co-writing of manuscript
Acta Cryst. **2017**, *C73*, 880-884	4.3	1st	support with conceptual approach, ana. work, co-conception and co-writing of manuscript
J. Am. Chem. Soc. **2016**, *138*, 13171-13174	4.4	1st	support with conceptual approach, exp. and ana. work (excluding ITC and XRD), co-conception and co-writing of manuscript
Angew. Chem. Int. Ed. **2017**, *56*, 15733-15736	4.5	1st	support with conceptual approach, exp. and ana. work, co-conception and co-writing of manuscript
Chem. Asian J. **2016**, *11*, 1597-1605	4.6	1st	conceptual approach, exp. and ana. work, DFT study (excluding XRD), conception and writing of manuscript
Dalton Trans., **2015**, *44*, 18329-18339	4.7	2nd	support of 1st author (D. Weiss) with method development and validation
Chem. Unserer Zeit **2015**, *49*, 260-269	4.8	1st	research, co-conception and co-writing of manuscript
Coord. Chem. Rev. **2017**, *352*, 517-536	4.9	2nd ‡	research, co-conception and co-writing of manuscript

7.3 Curriculum Vitae

PERSONAL DETAILS

Name:	Philipp Johannes Altmann
Date, place of birth:	07.02.1989, Eggenfelden
Contact:	Werner-Egk-Bogen 47
	80939 Munich
	philipp.altmann@mytum.de
	+49 170 7796543

EDUCATION

01/2015 – 02/2018 **Doctoral Studies in Chemistry**
Technische Universität München, Munich
Dissertation topic: *„Macrocyclic NHC ligands and their complexes for catalytic and supramolecular applications."*

10/2012 – 10/2014 **Master's Program in Chemistry**
Technische Universität München, Munich
Focus: Inorganic & metalorganic, organic chemistry;
Degree: Master of Science, overall grade: 1.0 (valedictorian)

10/2009 – 10/2012 **Bachelor's Program in Chemistry**
Technische Universität München, Munich
Degree: Bachelor of Science, overall grade: 1.6

07/2008 – 08/2009 **Army Service**
Reconnaissance Battalion 8, Freyung-Grafenau
Rank at end of service: Hauptgefreiter (Private 1st Class)

1999 – 2008 **Graduation**
Comenius-Gymnasium, Deggendorf
Degree: General University Entrance Qualification, grade: 1.7

PRACTICAL EXPERIENCE

01/2015 – 02/2018 **Scientific Staff / PhD Candidate**
Technische Universität München, Munich
Chair of Inorganic and Metalorganic Chemistry,
Tasks: Synthetic work (analytics *via* MS, NMR, IR, SC-XRD), composition of publications, scientific presentations, guidance and examination of students in various lab courses

09/2016 – 12/2016 **Guest Research Aboard**
University of Edinburgh, Edinburgh, Scotland
Crum Brown Chair of Chemistry,
Task: Synthesis of novel uranium and scandium compounds

02/2013 – 04/2013	**Guest Research Aboard**
	King Abdullah University of Science and Technology, Thuwal, Saudi-Arabia
	Physical Science and Engineering Division,
	Task: Design of biocompatible catalyst systems

03/2012 – 04/2012	**Industrial Internship**
	WACKER Chemie AG, Burghausen
	quality management sector,
	Tasks: Analysis of production samples, design of novel analysis methods

10/2010 – 12/2012	**Research Assistant**
	Technische Universität München, Munich
	Tasks: Synthetic and literature research

SCHOLARSHIPS AND AWARDS

09/2016 – 12/2016	**Short-term Scholarship** (DAAD) for the research stay aboard
07/2015	**Jürgen Manchot Award** for outstanding academic achievements
10/2013 – 10/2014	**Deutschland-Scholarship** (50% Fed. Republic of Germany, 50% Clariant)
02/2013 – 04/2013	**PROMOS-Scholarship** (DAAD) for the research stay aboard

VOLUNTEER WORK

08/2015 – 08/2016	**Elected speaker of the Chemistry Department Graduate Center of the TU München** (TUM Graduate School)
10/2009 – 12/2014	**Member of the student council of the Chemistry Department of the TU München** (Fachschaft Chemie der TU München e.V.)
Since 10/2007	**Certified track & field referee** (Deutscher Leichtathletik-Verband)
Since 02/2006	**Certified track & field C-coach** (Bayerischer Leichtathletik-Verband)

MISCELLANEOUS

Publications	**20 publications in scientific journals**, 8 as first author and 4 as second author, cumulated **Impact-Factor: 125.4** (as of 02/2018), talks and poster presentations at international conferences (*cf.* publications list)
Languages	German (mother tongue)
	English (fluent, GER level C2)
	Spanish (basic knowledge, GER level A1)
Hobbies	Sports (track & field, cycling, Frisbee, skiing), hiking, E-bass, Single-Malt-Whisky

Munich, February 16, 2018